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# BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 2 1961


## EXPERIMENTAL RESEARCH ON DIABETES MELLITUS*


BY

**F. G. YOUNG, M.A., D.Sc., F.R.S.**

*Professor of Biochemistry, University of Cambridge*


The research which is discussed in this article has been largely directed towards the experimental production in animals of a condition which resembles diabetes mellitus in the human being, together with the examination of the condition in animals and the investigation in human beings of certain points which arise as the result of the animal experimentation. I shall make no attempt to survey the whole of the vast field of research which is relevant, but shall largely consider the investigations of myself and my colleagues, although naturally I shall refer to some other researches.

### Experimental Pancreatic Diabetes

The discovery by von Mering and Minkowski in 1889 that surgical removal of the pancreas from the dog results in a condition which resembles severe diabetes mellitus in the human being, together with the observation that degenerative changes are seen in the islets of Langerhans of the pancreas of some diabetic patients (Opie), suggested the possibility that naturally occurring diabetes mellitus was caused by a defect in the mechanism in the pancreatic islets which normally produced a putative antidiabetic hormone.

Despite early failures, including those of Minkowski himself, to prepare the supposed hormone, by 1909 de Meyer (1909) was so confident of its existence that he named it "insuline." When in 1921 Banting and Best at last brought the elusive substance into the light of day the appropriateness of the already dubbed name, with only a slight emendation, was not long in doubt.

Insulin was obtained as a crystalline protein by Abel in 1926. Because the chemistry of proteins was a particularly difficult field of research, it was not until more than 20 years later that a systematic attack on the chemical structure of insulin was started. Then in the comparatively short period of 10 years—1945 to 1955—Dr. Frederick Sanger (see Sanger, 1960) and his colleagues at Cambridge completely elucidated the chemical structure of insulin from ox pancreas (Fig. 1), and subsequently he and his colleagues, of whom Dr. L. F. Smith has been most prominent in this respect, have determined the chemical structures of insulins from a number of species of animals. The clear-cut species differences in the chemical structure of insulin at present known are given in the Table.

*Species Differences in the Amino-acid Sequence of the Insulin Molecule*

| | A Chain | | | | B Chain | | |
|---|---|---|---|---|---|---|---|
| | 4 | 8 | 9 | 10 | 3 | 29 | 30 |
| Ox[1] .. | Glu | Ala | Ser | Val | Asp($NH_2$) | Lys | Ala |
| Sheep[2] .. | Glu | Ala | Gly | Val | Asp($NH_2$) | Lys | Ala |
| Horse[3] .. | Glu | Thr | Gly | Ileu | Asp($NH_2$) | Lys | Ala |
| Sei whale[4] .. | Glu | Ala | Ser | Thr | Asp($NH_2$) | Lys | Ala |
| Pig[2] .. | Glu | Thr | Ser | Ileu | Asp($NH_2$) | Lys | Ala |
| Sperm whale[3] | Glu | Thr | Ser | Ileu | Asp($NH_2$) | Lys | Ala |
| Dog[5] .. | Glu | Thr | Ser | Ileu | Asp($NH_2$) | Lys | Ala |
| Human[6] .. | Glu | Thr | Ser | Ileu | Asp($NH_2$) | Lys | Thr |
| Rabbit[5] .. | Glu | Thr | Ser | Ileu | Asp($NH_2$) | Lys | Ser |
| Rat 1[5] .. | Asp | Thr | Ser | Ileu | Lys | Lys | Ser |
| Rat 2[5] .. | Asp | Thr | Ser | Ileu | Lys | Met | Ser |

[1] Sanger and Tuppy (1951); Sanger and Thompson (1953). [2] Brown, Sanger, and Kitai (1955). [3] Harris, Sanger, and Naughton (1956). [4] Ishihara, Saito, Ito, and Fujino (1958). [5] Smith, L. F., unpublished. [6] Nicol and Smith (1960).

In these days when group activity, as opposed to that of the individual, is often rated of highest importance in scientific research, it is particularly pleasing that the problem of the chemical structure of insulin should have been solved not by a "team" of investigators "headed" by somebody, but by an individual who by choice pursued his researches with no more than one or two individuals at a time.

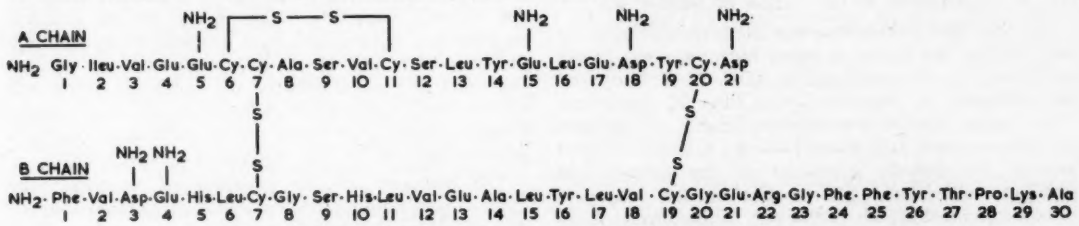
A CHAIN
B CHAIN
NH2 Gly·Ileu·Val·Glu·Glu·Cy·Cy·Ala·Ser·Val·Cy·Ser·Leu·Tyr·Glu·Leu·Glu·Asp·Tyr·Cy·Asp
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
NH2·Phe·Val·Asp·Glu·His·Leu·Cy·Gly·Ser·His·Leu·Val·Glu·Ala·Leu·Tyr·Leu·Val·Cy·Gly·Glu·Arg·Gly·Phe·Phe·Tyr·Thr·Pro·Lys·Ala
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

FIG. 1.—Structure of insulin from ox pancreas (see Table above for references).

Fortunately the chemical differences between insulins of different species are not commonly associated with cross-insensitivity to the action of the hormone. The parenteral administration to the human patient of insulin extracted from the pancreas of the ox or sheep, which differs chemically from that prepared from the human pancreas (see Table), normally effects satisfactory control of the human condition.

Because the nature of these chemical differences in insulins is now clear it is not surprising to find that in some instances insulin from one species is quite strongly

*A Litchfield Lecture delivered to the University of Oxford Medical School on May 17, 1961.

antigenic in another (Stavitsky and Arquilla, 1953; Moloney and Coval, 1955). Antisera to insulin thus produced have been used for the detection and assay of insulin in blood plasma (Yalow and Berson, 1957).

An interesting possibility is that a genetic defect in the pancreatic islets might result in the production of an insulin molecule which differed by perhaps only a single amino-acid from the normal for the species concerned. If such a defect occurred in a part of the insulin molecule which is vital for biological activity, a subnormally active or completely inactive molecule might partly or wholly replace normal insulin. This possibility is purely speculative at the present time (Young, 1959), but if such abnormal molecules exist they may be chemically detectable. An abnormal insulin might, unlike endogenous insulin, be antigenic, with the production of antibodies which reacted with both exogenous and endogenous insulin. A highly insulin-resistant diabetes mellitus might then develop. This is but one of many lines of thought which arise from precise knowledge of the chemical structure of insulin and its species variation.

Despite these possible complexities it is reasonable to suppose at the present time that a high proportion of patients who suffer from diabetes mellitus do so because their islets of Langerhans fail to secrete sufficient normal insulin for their needs. Even a slight deficiency of insulin could result in a small general rise of the blood-sugar level, and the hyperglycaemia so induced might then induce or exacerbate damage to the islets of Langerhans. In this way a severely diabetic condition could develop.

Nevertheless I think that at the present time few would dare to assert that diabetes mellitus always straightforwardly arises because of a subnormal production of insulin by the pancreatic islets. The reason for this caution is the growing evidence for the normal existence in the body of antagonists to the action of insulin, the excessive production of which might result in the development of diabetes mellitus even though the islets of Langerhans initially suffered from no defect.

### Antagonists to the Action of Insulin

The fact that a hormone can act physiologically by antagonizing the action of other hormones was firmly established by the investigations of B. A. Houssay and his colleagues in Argentina more than 30 years ago. They found that if the pituitary gland, or its pars glandularis alone, was removed from a depancreatized animal, the diabetic condition of the animal was strikingly alleviated and the life of the otherwise untreated animal greatly prolonged. Subsequently Long and Lukens found that experimental removal of the adrenal glands also depresses the severity of pancreatic diabetes, although some therapy with adrenal hormones may be needed to maintain the adrenalectomized-depancreatized animal in good condition.

Removal of the thyroid gland will also alleviate existing pancreatic diabetes in many species of animal (Houssay, 1948), although the effect of the removal of the thyroid gland is less striking than that of the pituitary or adrenal glands.

The alpha cells of the pancreatic islets secrete glucagon (Sutherland and de Duve, 1948; Foà, Galansino, and Pozza, 1957), a substance which may itself antagonize insulin in some respects, while the antagonism of adrenaline and insulin have long been recognized.

In the time at my disposal I shall single out one of these insulin antagonists for special attention—one of those present in the tissue of the anterior pituitary gland.

### Diabetes-inducing Action of Extracts of the Anterior Pituitary Gland

Houssay, Biasotti, and Rietti (1932) observed that the administration to a partially depancreatized dog of a suitable extract of the anterior lobes of ox pituitary glands could induce the appearance of a temporarily diabetic condition.

I began investigations in 1935 with intact dogs as test animals with the idea of isolating the diabetes-inducing pituitary substance and of investigating its mechanism of action. After some initial difficulties I found that in the intact dog the daily administration for one to three weeks of a simple extract of ox anterior pituitary would induce not only a temporarily diabetic condition but one which persisted indefinitely after treatment with the pituitary extract ceased (Young, 1937, 1938). In such animals no signs of the pituitary treatment permanently remained after cessation of the daily injections, apart from the induced diabetes. I can still recall the excitement with which we examined histological sections of the pancreases of these animals which had been prepared by Mr. K. C. Richardson, observing lesions in the islets of Langerhans which ranged from mild degranulation, through hydropsis of various degrees of severity, to complete hyalinization (Richardson and Young, 1938; Richardson, 1940).

A persisting diabetes had thus been induced by a short-lived treatment of a type which could be regarded as initially physiological, though ultimately the excessive emphasis of physiological processes had led to pathological changes in the insulin-secreting mechanism. The possibility could then be considered that human diabetes mellitus might sometimes arise from a short-lived period of hyperactivity of the anterior pituitary lobe, such as might not induce detectable signs of pituitary overaction other than the persisting diabetes. If this were so, search in the diabetic patient for the primary cause of the diabetic condition might prove to be fruitless because that cause might have disappeared by the time the condition had been diagnosed and the patient examined, the persistence of the condition being due to secondarily induced lesions in the pancreatic islets. I shall discuss later more recent investigations which provide support for the validity of this hypothesis.

The discovery of the existence of experimentally induced persisting pituitary diabetes, or metahypophysial diabetes as it subsequently was called, was made in 1937, but it was not until after the war that I and my colleagues were able to identify the substance in our ox pituitary extracts which produced this diabetes. We then concluded that it was pituitary growth hormone, or something closely associated with or formed from it (Cotes, Reid, and Young, 1949; Young, 1953; see also Young, 1939a, 1945). We used intact cats, rather than dogs, in our later experiments on the diabetes-inducing action of growth hormone, since we found that unfortunately this hormone shows its diabetes-inducing effects most constantly in carnivorous animals, and there were no other carnivorous laboratory animals available in sufficient numbers.

In our experiments prolonged daily treatment with growth hormone in doses which induced diabetes in the adult animal does not cause the appearance of a diabetic condition in young growing dogs and cats, but does stimulate excessive growth (Young, 1953). It is only when relatively large doses of growth hormone are given to the adult animal of a limited number of species—as I have just said, mostly carnivorous ones—that its diabetes-inducing activity is readily seen. Unfortunately, in our hands that useful laboratory animal the rat does not develop diabetes when treated excessively with growth hormone alone. Even elderly senile rats respond well to the growth-promoting stimulus of the injected hormone, with no sign of the development of diabetes. Recently the administration of human growth hormone to patients has been found to exert the diabetes-intensifying action expected on the basis of earlier experiments with animals (Ikkos and Luft, 1960).

In addition to growth hormone, pituitary corticotropin can exert a diabetes-inducing action under some conditions (Ingle, 1948; Conn, Louis, and Wheeler, 1948), as also can adrenal steroids with a ketonic oxygen atom or a hydroxyl group at position 11 of the molecule (Ingle, 1941, 1948). Corticotropin and adrenal steroids are in general less effective in inducing diabetes in those species, such as the cat and the dog, in which growth hormone is more active in this respect (Young, 1953; Abelove and Paschkis, 1954; Buse, Gundersen, and Lukens, 1957). The diabetes-inducing action in the dog of the crude extracts of ox pituitary extract used in the early experiments of Houssay and of myself is, I believe, attributable largely to the growth hormone contained therein (Young, 1953).

The diabetes-inducing action of growth hormone probably accounts for the fact that diabetes mellitus often complicates acromegaly, while the similar action of corticotropin and of certain adrenal steroids could account for the diabetes frequently seen in Cushing's syndrome.

### Estimation of Growth Hormone in the Blood Plasma of Human Patients

At Cambridge recently Ehrlich and Randle (1961a) have developed a method for the immunological assay of human growth hormone in blood serum which is based on the haemagglutination-inhibition method of Read (Read and Bryan, 1960). The serum-content of human growth hormone, assayed in this way, was found to be abnormally high in each of the seven untreated overweight diabetic patients examined (Ehrlich and Randle, 1961b). It was also elevated in three out of nine untreated underweight diabetics who had no ketoacidosis, and in only one out of nine untreated underweight diabetics in all of whom ketoacidosis was observed. In all of the 18 treated diabetic patients who had no complications the serum content of human growth hormone was in the normal range, but it was elevated in 8 out of 17 diabetics with retinopathy, and in five out of eight pregnant diabetic women. The values in non-diabetic pregnant women were in the normal range (Ehrlich and Randle, 1961a). Ehrlich and Randle (1961b) conclude that in the overweight untreated diabetic both the excessive weight and the diabetes mellitus may result from the observed rise in circulating growth hormone.

The finding that the circulating growth hormone is high in treated diabetic patients with complicating retinopathy is of great interest, and is in accord with the diminution in the severity of retinopathy which has been observed in diabetic patients in whom Sheehan's syndrome develops (Poulsen, 1953) or who are surgically hypophysectomized (Ikkos, Luft, and Gemzell, 1958).

These important observations of Ehrlich and Randle support the view that the oversecretion of growth hormone may be a factor of importance in the development of human diabetes mellitus in at least a proportion of those who suffer from this condition.

### Mechanism of Production of Metahypophysial Diabetes

When diabetes is produced in the intact dog or cat by the daily administration of growth hormone the appearance of hyperglycaemia and glycosuria, which do not occur for some days, is preceded by the development of a high degree of insensitivity to the hypoglycaemic action of a small dose of administered insulin (Young, 1939b, 1953). This condition of insulin insensitivity persists after the diabetes develops, and the administration of many hundreds of units of insulin may be needed daily to reduce the blood sugar back to a normal level once it has risen. When the daily treatment with growth hormone ceases and permanent (metahypophysial) diabetes is seen, the sensitivity to insulin rapidly rises (Fig. 2), though it usually remains slightly but significantly below that of the depancreatized dog (Marks and Young, 1939). When the dog with metahypophysial diabetes is depancreatized the insulin requirement usually falls (Marks and Young, 1939) (Fig. 2).

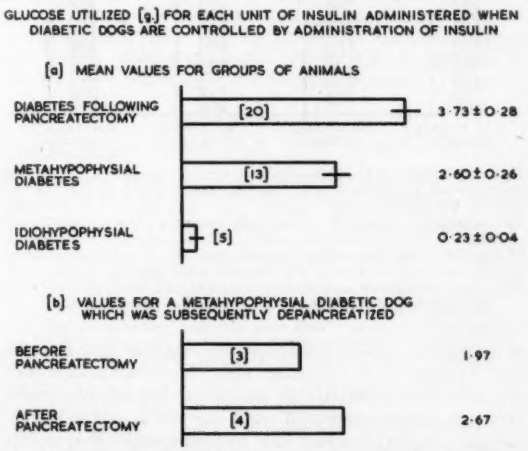


FIG. 2.—Insulin sensitivity of dogs with various types of diabetes. Based mainly on data in Marks and Young (1939). "Idiohypophysial diabetes" is used to indicate the diabetes in a dog under treatment with growth hormone. "Metahypophysial diabetes" is the diabetic condition which persists after the treatment with growth hormone. The figures in parentheses give the total number of observations made.

In the experiments of Mr. H. P. Marks and myself on this topic care was taken to ensure that the disturbed digestive function of the depancreatized dogs did not complicate the results. Such complications were avoided by feeding large amounts of raw pancreas to both depancreatized and metahypophysial diabetic dogs, faecal analyses being made to ensure that the adsorption of food from the gut was similar in both groups (Marks and Young, 1939). Thorogood and Zimmermann (1945) and Rodriguez-Candela (Rodriguez-Candela, 1945;

Rodriguez-Candela, Goñi, Caldeiro, and Gonzalez Carreras, 1947) observed a fall in insulin requirement when alloxan-diabetic dogs were depancreatized, although in these experiments the adequacy of absorption of food from the gut of the depancreatized dogs was not ensured (see Mirsky, Futterman, Wachman, and Persutti, 1951 ; Rodriguez-Candela, 1952).

Though it is small the difference in insulin requirement between dogs with metahypophysial diabetes and depancreatized dogs observed in our experiments appears to be significant. What is the reason for it ? The alpha cells of the pancreatic islets usually remain when metahypophysial diabetes develops, and the secretion of glucagon by them might provide an explanation of this observation, although other possibilities cannot be ruled out.

The gross insensitivity to the hypoglycaemic action of insulin which is seen during the period of treatment with growth hormone can reasonably be related to the reduction in response of rat diaphragm to the *in vitro* addition of insulin when the rat has previously been treated with growth hormone (Cori, 1950). Fig. 3, which

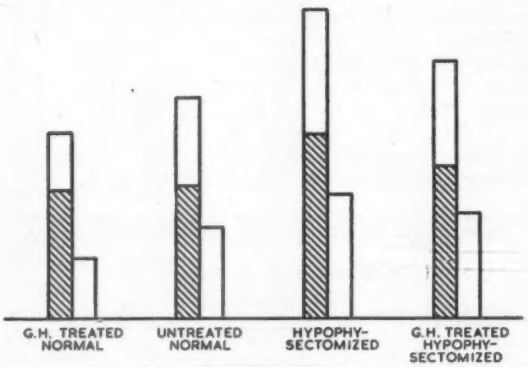


FIG. 3.—Effect of hypophysectomy, and of treatment of the rat with growth hormone (1 mg./day for seven days) on the glucose uptake of subsequently excised and isolated rat diaphragm. GH.=growth hormone. Hatched columns=basal uptake of glucose. Blank columns=addit.onal uptake when insulin (0.5 milliunit/ml. of medium) added *in vitro*. The blank columns are drawn both on top of the hatched ones and on the baseline. The latter facilitates comparison between the various groups of the effectiveness of insulin in promoting glucose uptake.

is based on results published by Manchester, Randle, and Young (1959), illustrates this phenomenon and also the enhanced sensitivity to insulin *in vitro* of diaphragm from hypophysectomized rats, and the reduction in insulin sensitivity when the hypophysectomized rat is treated with growth hormone. Unfortunately, in experiments of this sort the addition of growth hormone *in vitro* to rat diaphragm does not consistently or significantly diminish the sensitivity of the tissue to insulin added *in vitro*. It seems that growth hormone is not itself the insulin antagonist, but something formed from it. The nature of this substance is not at present clear (see Bornstein and Hyde, 1960 ; Vallance-Owen and Lilley, 1961) though it may be formed from growth hormone as the result of a metabolic degradation.

As I mentioned earlier, the diabetic state induced in the dog or cat by the daily administration of growth hormone usually does not appear until after several days of treatment, yet during this latent period gross insensitivity to the action of administered insulin may exist. At the same time mitotic activity, as well as degenerative changes, may be seen in the beta cells of the pancreatic islets (Richardson and Young, 1938 ; Richardson, 1940). This insensitivity to exogenous insulin in the absence of a rise in blood-sugar level (see Young, 1939b) may well reflect a temporary suppression of any effect of the low sensitivity to endogenous insulin on the blood-sugar level by a compensating increase in the rate of secretion of insulin by the islets of Langerhans. Calculation suggests that the pancreatic islets might at this time be secreting many times the normal amount of insulin in order temporarily to keep down the blood-sugar level. Under these conditions the addition of a small test dose of endogenous insulin to that already circulating might well have little or no effect on the blood-sugar level.

If this interpretation of the experimental observations is correct it might reasonably be supposed that when the blood-sugar level ultimately rises under the influence of treatment with growth hormone the rise reflects an inability of the pancreatic islets to continue to secrete insulin at an abnormally high rate. The observed degenerative changes in the beta cells of the islets of Langerhans and the development of metahypophysial diabetes might thus result from permanent damage to the islets occasioned by this temporary overstrain.

These suggestions carry the implication that under the influence of treatment with growth hormone the pancreas may be induced to increase its secretion of insulin. What is the evidence for this ?

### Growth Hormone and the Secretion of Insulin

At Cambridge Dr. P. J. Randle has developed a method for the assay of plasma insulin activity (Randle, 1954a, 1956) which is based on the use of the rat diaphragm *in vitro* as first applied to the assay of insulin by Groen, Kamminga, Willebrands, and Blickman (1952). By this means Randle has found that the insulin-like activity of the plasma from acromegalic patients is frequently elevated (Randle, 1954b) while that in patients with hypopituitarism is usually depressed (Randle, 1954c). Randle and Young (1956) found that treatment of the intact cat with growth hormone greatly increased the insulin activity of the blood plasma, but no rise was observed when the depancreatized cat receiving a constant daily dose of insulin was similarly treated. It seemed therefore that the rise in plasma insulin activity under the influence of growth hormone depended upon the presence of the pancreas and was not due to a depression of the rate of inactivation of circulating insulin. The simplest conclusion was that treatment with insulin had indeed stimulated the secretion of insulin by the pancreas. Nevertheless it seemed desirable to obtain more direct evidence by examination of the plasma of the blood draining from the pancreas itself.

### Plasma Insulin Activity in Pancreatic Venous Blood

In 1953 Dr. Randle and I together set out to investigate the insulin activity of the plasma of the venous blood which drains from the pancreas of cats that had been made diabetic by treatment with growth hormone. The insulin activity of the blood plasma was assessed by its stimulating effect on the glucose uptake of the isolated rat diaphragm, and by the induced fall of blood sugar when the plasma was injected intravenously into alloxan-diabetic hypophysectomized rats. We found to our surprise that there was less insulin activity in

the plasma from the blood of the portal than in that of the femoral vein, and this was true not only for cats which had been made diabetic by treatment with growth hormone but also for normal control cats (Randle and Young, unpublished results). The problem therefore appeared to be a complicated one and we abandoned it at that time.

Much later I returned to this problem (Young, 1961), using for the assay of insulin activity in blood serum the glucose uptake of rat diaphragm or of rat adipose tissue. In experiments with normal cats I found that the serum of the venous blood draining the pancreas contained less insulin activity than that of the femoral artery (Young, 1961). I was loath to accept the view that the pancreas destroys rather than secretes insulin, and therefore investigated the possible influence of the degree of oxygenation of the blood on the insulin activity of the serum prepared from it. With slaughter-house blood oxygenated or deoxygenated *in vitro* it was found that oxygenation of the blood increased the insulin activity of the serum prepared from it, while deoxygenation diminished it (Young, 1961). Essentially similar results were obtained *in vitro* with blood from the cat, pig, horse, rabbit, and human being. Oxygenation and deoxygenation of separated serum or plasma had no similar action, and the effect appeared to depend upon the presence of the blood corpuscles.

Fractionation of the plasma proteins from oxygenated and deoxygenated blood showed that the biggest difference in insulin activity lay in the gamma-globulin fraction (Gardiner, Martin-Hernandez, and Young, 1960). A smaller difference was observed in the albumin fraction, though this may make an important contribution to the effect of the whole serum or plasma, since in our experiments the albumin fraction constituted about 60% of the total plasma protein (Gardiner *et al.*, 1960).

In some instances the addition *in vitro* to rat diaphragm of the gamma-globulin fraction from deoxygenated blood depressed the glucose uptake of the diaphragm, whereas the addition of the gamma-globulin from a sample of the same blood which had been oxygenated *in vitro* enhanced the glucose uptake of the diaphragm. Thus oxygenation of the blood had transformed an insulin-inhibitory action of the plasma gamma-globulin fraction to an insulin-like one (Gardiner *et al.*, 1960). For this and other reasons it seems probable that the effect of oxygenation is to restrain the activity of the insulin inhibitor, the restraint being released when the blood is deoxygenated or becomes venous. These results provide a reasonable explanation for the observed fact that the biologically assessed insulin-activity of the serum or plasma from the venous effluent of the pancreas is less than that of serum or plasma from arterial blood.

Oxygenation *in vitro* of the venous effluent from the pancreas appears to raise the insulin activity of the serum above that of the serum of arterial blood, but whether treatment of the animal with growth hormone raises it further is a matter still under investigation.

## Conclusion

Plasma insulin activity in animals rises when growth hormone is administered under suitable conditions, while elevated values for plasma insulin activity are observed in the human being in conditions where the endogenous secretion of growth hormone is likely to be raised. In untreated diabetic patients, and in many treated patients who have complicating retinopathy, abnormally high levels of serum growth hormone are observed. These observations, together with the fact that the daily administration of growth hormone to dogs and cats for a short time can induce a diabetic condition which persists after the treatment with hormone is stopped, reinforce the view that oversecretion of growth hormone during a short period of time may be one cause of human diabetes mellitus (Young, 1938, 1939a).

For the induction of a persisting diabetes mellitus the oversecretion of growth hormone might need to be of only short duration and need cause no signs of acromegaly. Indeed, the only permanent stigmata might be damage to the islets of Langerhans with consequent persisting diabetes mellitus.

In most instances the primary cause of the diabetic condition—namely, a short period of oversecretion of growth hormone—might well have disappeared before the diabetic condition is recognized and a search for its primary cause begun. In other instances—for example, in diabetic retinopathy—it may linger on in the form of an elevated serum growth hormone content, and this might be a cause of the complications seen in this condition.

The promotion of growth may indeed be but one aspect only of the manifold actions of the metabolic regulator called pituitary growth hormone.

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# PSYCHIATRIC ASPECTS OF EPILEPTIC AND BRAIN-DAMAGED CHILDREN*

BY

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## Brain Damage

The concept of the brain-damaged child that has been steadily gaining ground in the last few years merits careful and critical examination. Contributions to it have been made by a number of authors—for example, Bradley (1957), Strauss and his co-workers (Strauss and Lehtinen, 1947; Strauss and Kephart, 1955), Bender (1956), and, most recently, Eisenberg (1957), whose review of the symptoms may be taken as one of the clearest expositions of the clinical concept. The symptoms said to be most commonly associated with brain damage in children are hyperkinesis, distractability and short attention-span, lability of mood, antisocial behaviour, low intelligence, and anxiety. These are diffuse symptoms in the sense that they affect large areas of mental functioning, though it is uncertain whether the responsible lesions are diffuse or focal—for example, in the temporal-lobe or mid-brain regions.

The criteria for brain damage appear to be as follows:

1. *History:* which may be of a head injury, encephalitis, anoxia at birth, meningitis, or many another trauma or inflammation of the brain and its coverings. This history may be good evidence of brain damage in the past, but there is the obvious danger of *post hoc, ergo propter hoc*, when it is claimed as the cause of subsequent symptoms.

2. *Neurological Signs and Symptoms such as Hemiplegia or Hemianopia.* These symptoms are signs of damage of a particular part of the brain. Their absence does not signify the absence of brain damage elsewhere, nor does their presence necessarily imply that the damaged area producing these symptoms may also be responsible for the other psychiatric symptoms of which the patient complains.

3. (*a*) *Special Investigations: Physical* (*A.E.G. and E.E.G.*).—The air-encephalogram is a coarse test of brain damage and sometimes shows normality even when surgery or necropsy has subsequently shown clear evidence of brain damage. The interpretation of the E.E.G. contains even more pitfalls, because there is certainly no E.E.G. change pathognomonic of diffuse brain damage. The findings of an excess of slow activity in an E.E.G. of a patient with a past history of brain damage cannot be regarded as unequivocal evidence of a continued physiological disturbance from that brain damage (see Cobb, 1950). Furthermore, in children there is a very wide variation in standards of normality at any one age, making interpretation still more difficult.

3. (*b*) *Special Investigations: Psychological.*—An adequate survey of the psychological test investigations in brain damage would occupy a lecture in itself (see reviews of Meyer, 1960; and O'Connor, 1958). There would seem to be three main groups of tests. The first refer to the use of special indices in the standard intelligence tests of Wechsler or Binet. Measures of deterioration in adults by comparing the verbal and performance scores are well recognized and standardized. Their application in children is more difficult, since on the one hand wide discrepancies may be found between verbal and performance scores in patients in whom brain damage is not suspected, and on the other no such discrepancies may be found in children with undoubted brain damage. Educated parents can produce a spuriously high verbal score in their backward children.

The second group of tests are those concerned with special psychological functions, of which those related to perceptual anomalies seem to be the most important—for example, the Bender-Gestalt, various form-board tests, etc. Unfortunately, most of these tests have been poorly standardized with inadequate controls. Moreover, often there are no clear correlations between the test results and, on the one hand, the neurological status, and, on the other, personality difficulties and maladjustment (Cruickshank and Bice, 1955).

The third group of psychological tests are the so-called projection tests, of which the Rorschach is the one most frequently used. Many authors have described specific organic signs in the Rorschach test, but these have been equally often denied, and the whole status of this test, and therefore, by implication, of other projective tests, is at the moment under a cloud (Tizard, 1961).

These strictures on the dubious value of most psychological tests should not be regarded as decrying the function of the psychologist himself. In fact, it somewhat increases it in that he or she is essential for the empirical study of any particular case, especially as regards the practical problems of the treatment of a damaged child. By patient investigation of what a child can or cannot do—in, for example, the learning situation—the psychologist makes an essential contribution which cannot be carried out in any other way, but which has a much more dubious connexion with the theoretical problems. For example, the works of Strauss and Lehtinen (1947) and Strauss and Kephart (1955) are deplorably diffuse, irrelevant, and inaccurate, but their insistence on the study of the individual case and their conclusions about teaching methods of handicapped children are important.

There are thus no absolutely unequivocal clinical signs, physiological tests, or psychological tests that can

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prove a relationship between brain damage and any particular aspect of disturbed behaviour. The position is much less certain than in the case of epileptic phenomena, since there are numerous opportunities, clinically and experimentally, of recording the abnormal electrical activity of the nervous system in a fit, at the same time as observing the abnormal behaviour of subjects in the throes of an epileptic discharge.

### Clinical Survey of Brain-damaged Children

I have recently begun a survey of the children seen at the Maudsley in whose clinical state organic factors were considered to be important. It at once became apparent that the majority of such children were of below average intelligence, often at the lowest grades. Of such cases I chose only those in which the aetiology was clear-cut, and most of them were fully investigated as in-patients. All those who had epileptic attacks of any sort at any time were excluded.

The adoption of these strict criteria produced relatively few cases, scattered over a number of years. The analysis given in Table I is based on the first 58 obtained from the records.

TABLE I.—*Brain-damaged Children Without Epilepsy* (*Males*, 40; *Females*, 18)

| | | | |
|---|---|---|---|
| **Evidence for brain damage:** | | **Age when brain damage suffered:** | |
| History only | 30 | 0–1 year | 35 |
| Physical signs | 21 | 2–4 years | 8 |
| A.E.G. | 4 | 5–9 ,, | 7 |
| E.E.G. | 3 | 10+ ,, | 2 |
| | | Not known | 6 |
| **Intelligence level:** | | **Age when first seen at Clinic:** | |
| Less than 50 | 8 | | |
| 50–79 | 21 | | |
| 80+ | 29 | | |
| Significant discrepancies | 11 | | |

| Age when first seen at Clinic: | No. | Expectation from Total Clinic Cases |
|---|---|---|
| 2–4 years | 3 (5%) | 6% |
| 5–9 ,, | 21 (36%) | 23% |
| 10–14 ,, | 28 (49%) | 45% |
| 15+ ,, | 6 (10%) | 26% |

In order to assess the significance of the clinical data I have compared some of the facts with an unpublished dissertation of Dr. Q. Grant. He investigated a consecutive sample of non-organic children referred to the Maudsley Clinic with special reference to the age-and-sex distribution of their symptoms. He based his work largely on the method of McFarlane *et al.* in their excellent longitudinal survey of normal children in California.

In my series males outnumbered females more than 2 to 1, which is about the same as in the clinic generally. The intelligence range showed half the patients to have an I.Q. of less than 80, the usually accepted lower limit of the " normal " range. Only 11 of the children showed anomalous test results, either on the routine psychological tests or on the special tests such as the Strauss marble board, the Benton, etc.

The onset of the brain damage was in more than half the cases under 2 years of age, birth events being by far the largest single cause. Of the rest, meningitis, encephalitis, and head injury were the main causes. In contrast to the age of onset, the ages at which the patients were first seen at the clinic were some years later, mostly between 5 and 14 years, the peak periods for the ordinary clinic population (Table II).

As regards the background of the cases, the social-class distribution shows an excess of social class I, which may be due to the greater concern of educated parents for their children, or—less charitably but more plausibly

TABLE II.—*Brain-damaged Children Without Epilepsy* (58 *Cases*)

| Social class | Total | Expected |
|---|---|---|
| I | 8 (14%) | 4·7% |
| II | 9 (16%) | 16·2% |
| III | 18 (31%) | 55·1% |
| IV | 13 (22%) | 10·7% |
| V | 8 (14%) | 13·3% |
| Not known | 2 — | — |

| Environment | |
|---|---|
| Normal home | 13 |
| Broken ,, | 13 |
| Institution | 4 |
| Other relatives mentally ill | 16 |
| Abnormal parental attitudes | 30 |

| | Age of Brain Damage | | | | | Age when Seen at Clinic | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 0–1 | 2–4 | 5–9 | 10+ | N.K. | 2–4 | 5–9 | 10–14 | 15+ |
| Hyperkinesis | 8 | 2 | 1 | 0 | 2 | 2 | 8 | 3 | 0 |
| Aggression | 11 | 4 | 2 | 0 | 2 | 2 | 7 | 10 | 0 |
| Neurotic symptoms | 15 | 4 | 5 | 0 | 5 | 0 | 10 | 16 | 3 |

—because such parents cannot reach down to the level of these children and so often handle them badly. Only 13 children came from normal homes—that is, with both natural parents present and neither suffering any overt psychological illness or abnormal attitudes to the child. In half of the cases the parents, especially the mother, grossly overprotected or rejected the child, or showed some other abnormal attitude. The interpretation of parents' attitudes is based in most cases on the notes of many interviews between parent and doctor or psychiatric social worker. The bias is therefore that of the whole clinic, and it is open to the objection that psychiatrists think few people are normal. However, in addition, a third of the children were or had been for years in institutions or hospitals, or had come from broken homes with one or both parents missing, step-relations, etc. About one-quarter had close relatives who were psychiatrically ill.

As in the case of epilepsy, the symptoms are extraordinarily varied, and it is clear at once that the classical syndrome of the brain-damaged child does not cover more than a few of the children seen. Of the numerous symptoms present, only three groups are common enough to be analysed. They are: neurotic symptoms, abnormal aggressiveness (temper tantrums, cruelty, etc.), and hyperkinesis or restlessness.

Table III shows that the age of sustaining brain damage in these symptom-groups does not differ from the average of the whole group. However, the ages at which the patients were seen at the clinic show that hyperkinesis is commoner at the younger ages, aggression right through the middle ages, and neurotic symptoms in adolescence. We may compare this distribution with that found for similar symptoms by Grant in the non-organic population of the Maudsley Child Guidance Clinic. He found a peak for over-activity at ages 5–7 years in boys, for aggression at a similar age, and again in adolescence, and for neurotic symptoms from 11 to 13 years. Neurotic symptoms are

TABLE III.—*Brain-damaged Children Without Epilepsy*

| | Male | Female | I.Q. <80 | I.Q. 80+ | Abnormal Parental Attitude: Present | Abnormal Parental Attitude: Absent |
|---|---|---|---|---|---|---|
| Neurotic symptoms: | | | | | | |
| Present | 21 | 8 | 11 | 18 | 15 | 14 |
| Absent | 19 | 8 | 18 | 9 | 15 | 12 |
| Abnormal aggressiveness: | | | | | | |
| Present | 17 | 4 | 8 | 11 | 12 | 7* |
| Absent | 23 | 14 | 20 | 18 | 17 | 20 |
| Hyperkinesis: | | | | | | |
| Present | 12 | 1 | 10 | 3 | 6 | 7* |
| Absent | 28 | 15 | 19 | 24 | 21 | 22 |

* All with abnormal homes.

seen in both sexes, but are more common in those with higher (that is, normal) I.Q.s than lower. Abnormal aggressiveness is unrelated to intelligence, but is more common in boys than in girls. Not one of the children with those symptoms came from a normal home. Thirdly, hyperkinesis is most common in low intelligence, in boys much more often than girls, and again none of these children came from normal homes.

Thus the findings of Grunberg in epileptic-behaviour problem-children are closely paralleled by those with brain-damaged children; that is, as regard the type of symptoms, their age distribution, and the prevalence of disturbed environments, the brain-damaged child differs little from the ordinary child psychiatric population, *except* for the factor of low intelligence.

It would appear that the symptoms that bring a brain-damaged child to a psychiatric clinic are very similar to those for which non-brain-damaged children are brought. This type of survey cannot, of course, disclose how common these symptoms (and others) are in brain-damaged children generally, nor whether the brain-damaged child has other symptoms or defects not detected by our child psychiatric methods.

As regards the first point, only surveys of unselected samples or follow-up studies are appropriate. Several studies have shown that head injuries in children produce few long-term ill-effects even when they have been very severe and the patient has been very disturbed immediately afterwards (see Harrington and Letemendia, 1958). On the other hand, children with the permanent neurological defects that have led to their being classified as cerebral-palsied children are often emotionally disturbed. Dunsdon (1952) thought more than one-third were unstable, especially those with an I.Q. below 70; and Floyer (1955) thought nearly half showed some of the psychiatric symptoms said to be typical of the brain-damaged child.

Another study bearing on the prevalence of psychiatric symptoms in brain damage is Tizard's (unpublished) survey of mental defectives at home and in institutions, which covered children and adults; and, of course, some of the patients may not have had an acquired brain damage in the sense used here. He found that the only common, important, and easily assessable trait was underactivity or overactivity. 25% of the children were regarded as overactive, 9% as underactive. Only 41% were regarded as normal in temperament. It is also interesting to note that in adult defectives the problem of activity is reversed: 28% are underactive, only 12% overactive—a change similar to that which I have already mentioned in epileptic children.

These surveys can be regarded as no more than preliminary and merely showing how large a problem there is. There are so many variables that must be allowed for. For example, the factors of age, intelligence level, and presence of other physical disabilities in the child and in its environment, and the quality of parent or institutional care, are just a few that spring to mind at once.

The second point I mentioned concerns the possibility of there being psychological symptoms not shown by our psychiatric methods—especially, of course, the possibility of focal disorders of speech, motility, perception, and so on. In the case of children, many people consider that there is no such thing as a focal disturbance of function with a focal lesion of the cerebral hemispheres. This is manifestly untrue in the case of the simple uncomplicated cerebral palsy which may affect only one limb. Even at higher levels the problem may not seem so simple; for example, with acute lesions such as abscesses or open head injuries aphasia undoubtedly occurs in children, but it never results in a logorrhoea, as can sometimes occur in adults (Guttmann, 1942). Rather the child is more or less speechless, even completely mute. It is obvious that in general an early lesion in childhood may lead to failure to acquire patterns of behaviour, and this may have repercussions in many other ways. (A simple and obvious example is the effect of a peripheral lesion causing deafness that will lead to a failure to acquire speech if it is not tackled early and energetically.)

In the Maudsley material suspected aphasias are very rare—no more than three or four in more than ten years—and psychogenic mutism on the top of brain damage seems commoner. The impression that focal disorders of all sorts are rarely the sequel of brain injury is confirmed by the literature on such disturbances as reading disabilities or so-called congenital auditory imperception, etc. Few, if any, of such cases seem to be related to brain damage unless the disorder is part and parcel of a general mental deficiency. Many of them are inextricably mixed up with a general emotional disturbance, so it is hard to sort out which came first.

It seems that in our present state of knowledge we can say that in a general way the brain-damaged child is handicapped—in the first place, and without any doubt, as regards intelligence. Secondly, such children may suffer from defects of personality that are much less clear-cut, but probably concern all aspects, such as tolerance of anxiety, controllability of primitive impulses, and so on. As our methods of localizing brain damage at the cortical level are so poor, no useful analysis of the effects of different types and sites of brain damage can be made as Nuffield could with epilepsy. In any case, I very much doubt if there are any specific psychiatric entities such as the post-encephalitic, the post-traumatic, and so on, except in so far as there is also focal damage producing focal symptoms at a neurological level, such as a paralysis or a special sense loss, thus adding a particular contribution to the general handicap.

### Influence of Environmental Factors Before the Brain Damage

The environmental factor enters into the problem of the effects of brain damage in an even more fundamental way than the handling subsequent to the injury. In the last few years evidence has accumulated showing that the prevalence of premature births and other medical conditions of childhood possibly related to brain damage are not distributed randomly in the population but are concentrated in the lower social classes. For example, Douglas (1960), following up the premature babies in his very big prospective survey, found that they were inferior in their school and social progress but that this inferiority was clearly correlated with the social status of the parents and the general quality of maternal care rather than with the brain damage that may have been presumed to result from prematurity. Fairweather and Illsley (1960) found similarly that among the 66 children in Aberdeen's school for the educationally subnormal there was a high incidence of obstetric abnormalities, but in all these cases the families were from the lower social classes

with poor standards and often low intelligence, so that the authors felt there was no need to postulate birth trauma as a cause of the mental handicap.

In the last few years Pasamanick, Lilienfeld, and colleagues have published several papers on what they call prenatal and paranatal factors in the production of cerebral palsy, epilepsy, and behaviour disorders. They postulate a "continuum of reproductive casualty." On the face of it their work is impressive, with a careful control series for comparison with the cases taken from the same schools. However, the social factors are not adequately controlled. For example, the monograph of Rogers, Lilienfeld, and Pasamanick (1955) on behaviour-problem children shows a table of the number of families known to the Baltimore social service agencies. A highly significant larger number of the white cases, as opposed to the white controls, are known to the agencies. (Of the smaller number of non-whites, three-quarters of both cases and controls are known.) Similar differences appear in the problem children which they call misleadingly "hyperactive, confused-disorganized." Until the social status and quality of parental care of these children is properly controlled, no firm conclusions can be drawn about the significance of the organic factors.

(The contrast between these surveys and my hospital figure of excess of class I is due to the clinic being a selected sample and illustrates the fallacies of hospital data.)

The sorting out of constitutional *versus* environmental factors is a routine problem in psychiatry, and ordinary family history studies are of dubious value. Twin studies are the only reliable method. Thanks to the extremely complete statistics on the comparatively static population of Sweden, Dencker (1958) was able to collect a large series of twins, one of whom had sustained head injury severe enough to warrant admission to hospital. These twins were, of course, of all ages at the time of the injury and at the time of the examination. The follow-up in most cases was many years after the injury. Dencker interviewed both the proband and the control twin, and in a smaller number of pairs psychological tests were administered to both twins by Löfving (Dencker and Löfving, 1958).

Dencker was particularly interested in the so-called post-traumatic syndrome, and his work suggests strongly that persistent psychiatric symptoms which occur after injury have little relationship to the severity of the injury but a much closer relationship to the previous personality. He showed, for instance, that in most cases the uninjured identical twin tended to have similar symptoms, though usually in a milder degree. Löfving's tests showed up very small differences that were apparent only when the uninjured twin was used as a control. The test results obtained were in most cases within the normal range, but it did appear in general that the injured twin was slightly slower in many forms of responsiveness. In addition to these changes in psychological tests being very slight, there was also no obvious correlation between the severity of the changes and the severity of the general psychiatric picture. Dencker's paper refers to closed injuries only; hardly any of the patients developed epilepsy, and there were very few signs of focal brain damage.

Dencker's work does not adequately analyse the possible effects of environmental pressures in these similarities and differences. Identical twins have notoriously their own problems and tend to be treated somewhat alike. Interestingly enough, the investigation of Shere, quoted by Cruickshank and Bice (1955) on a small series of identical twins, one of whom had brain injury from birth or other early cause, would suggest that in some cases the uninjured twin showed more evidence of psychological disturbance. The reason for this, she plausibly argues, is the differential handling of the children by their parents, who would tend to favour the handicapped child, so that the non-handicapped one may well feel rejected and react accordingly. These observations are, of course, strongly in favour of the predominant importance of environmental factors.

The assessment of the long-term psychological effects of brain damage is therefore more complicated than it appears at first. The age and previous character of the person suffering the brain injury, and the ways in which he is subsequently handled, are the main factors determining the nature, severity, and duration of symptoms. Only in the case of intelligence, and possibly related traits such as viscosity or slowness, does there seem to be an important direct effect of the brain damage, and then the effects appear to be quantitative rather than qualitative, and proportional to the amount of brain damaged rather than its site and nature.

What we do not know are, firstly, the right personality traits to investigate in any constitutional twin studies designed to throw light on how people react to brain damage; secondly, we do not know the correct formulation of the effects of brain damage even as regards intelligence, since our present psychological tests often give equivocal or negative results. As regards the third factor—namely, the analysis of the effects of environmental handling—we are a bit further on, since the generally accepted concepts of child–parent relationships used in everyday child-guidance work help us not only to understand but also to treat brain-damaged children.

### Animal Experiments

Before attempting any further formulation of the effects of brain damage, brief consideration should be given to the results of certain animal experiments, especially those involving the deep temporal-lobe structures and the mid-brain reticular regions, the two areas with which we are particularly interested as regards behaviour and epilepsy.

The idea that the deep temporal-lobe regions may be connected with the expression of the emotions was put forward before the war by Papez (1937), but only in the last few years has the clinical and experimental evidence of this been clearly forthcoming. As in the case of the human observations, the behaviour disturbances in animals seem, in fact, to be related to three fields: firstly, the physiological expression of the emotions; secondly, the recent memory and learning of the new material; and thirdly, consciousness.

The work on the somatic expression of the emotions has recently been reviewed by Ursin (1960). Of the three common patterns of emotional behaviour seen in mammals below man—namely, rage, fear, and pleasure—only the first two are seen as the result of stimulation of the amygdaloid and probably the hippocampal regions. On the other hand, stimulation of comparable areas in the human at operation occasionally may produce the reaction of fear but rarely that of rage, and the responses seen are usually more complex and involve disturbances of consciousness. Williams (1956) found

that the content of epileptic auras is nearly always that of fear or depression and rarely rage. (The rage reactions found in chronic epileptics, as a form of interictal behaviour rather than ictal or pre-ictal behaviour, are different, as already mentioned.)

The effects of ablation of the deep temporal regions in animals are actually very varied. Green *et al.* (1957) mentioned 29 often contradictory varieties of behaviour that have been reported. Sexual activity is in the majority of cases increased as the result of these lesions, often with perverse tendencies as well. Green and Kaada both think there is some evidence of localization of function within the amygdaloid region, but there is as yet no convincing human clinical evidence on this point. Several authors (for example, Fuller *et al.*, 1957) have stressed that the circumstances under which the behaviour of the animals with brain lesions is studied is also of importance—a fact which, of course, agrees closely with clinical observation of human cases. In addition to the changes in respect of emotion, Green *et al.* (1957), for example, think that many of the changes in the behaviour seen with amygdala lesions in cats are due to disturbances of consciousness, and he compares their activity with disturbances of behaviour seen in psychomotor epileptics.

Experimenters with a different theoretical bias have been interested in the effects of lesions on the acquisition of new behaviour patterns—that is, learning and conditioning—rather than on the emotional reactions seen with stimulation or frustration. In the past no convincing evidence of any localization of such functions at the cortical level had been obtained, but, following on the observations of Penfield and Milner (1958) and Meyer (1959) on temporal lobectomy patients, Stepien *et al.* (1960) have recently obtained evidence that deep temporal lesions do impair particular types of new learning.

The work on the mid-brain reticular region centres around two closely interrelated problems. Firstly, there are those of consciousness, or level of activity, or awareness of the whole organism ; and secondly, the problem of the regulatory mechanisms, particularly of metabolic activity ; that is, there are both upward and downward influences from the reticular regions. Furthermore, the level of attention or activation or vigilance of the brain is maintained partly by the inflow of sensory information, but also by cortico-fugal impulses. Thus, the brain exerts some selectivity not only on the extent to which it will respond to incoming signals but also on the strength of the incoming signals themselves, though it is as yet uncertain how far down the sensory pathways central control can be exerted.

Most of the animal experimenters seem as far off a general theory of explanation of the effects of brain damage and epilepsy as are the workers on human material. I personally find very satisfying and stimulating the concepts of central-nervous-system function that derive from so-called "information theory." Pribram (1960) recently reviewed some of the applications of this type of theory. Hyperkinesis, for example, may be related to a failure of the homoeostatic mechanisms that are designed to keep the sensory information within manageable limits. The simplest analogy of the homoeostat is the thermostat, which keeps the temperature of a room constant. If the thermostat is very sensitive then the heat-source has to be turned on and off every few seconds. When we speak of a hyperkinetic child as being stimulus-bound we refer to the same sort of close tie between stimuli and the responses thereto. But a thermostat is also adjustable in the sense that the temperature at which the room is maintained can be altered. In the same way, we see that in patterns of sleep, wakefulness, underactivity, and overactivity the whole brain may react more or less to incoming stimuli. Such an idea may perhaps be related to the disturbances of sleep that these children show, since they are very often slow to go off to sleep and then go very profoundly and deeply asleep. This rhythm of sleep and wakefulness is less related to light and darkness and the other rhythms of daily life to which normal children get adjusted.

So far as the clinical effects of epilepsy in these regions are concerned it was, of course, the relationship of bilaterally synchronous and symmetrical spike-and-wave to loss of consciousness without other clinical accompaniments that first led the Montreal school to the concept of the centrencephalic system. The possible connexion of generalized epileptic activity to homoeostasis was actually put forward independently by Denis Hill (1952) some years ago in an article comparing and contrasting maturation disturbances in the E.E.G. with what he called homoeostatic phenomena. In support may be cited the therapeutic effects of electric shock treatment, provided the patient has a proper grand-mal attack. Possibly also the self-stimulating photosensitive patients have discovered a similar regulating mechanism. (On the other hand, the famous Maudsley patient who deliberately obtained sexual satisfaction culminating in an epileptic attack by the contemplation of open safety-pins had undoubted temporal-lobe epilepsy, so one cannot impute regulatory functions only to centrencephalic epilepsy (Mitchell *et al.*, 1954).)

I do not think that the animal experiments so far provide a clear answer to the question about any extra part that might be played by the lesions that are epileptogenic rather than non-epileptogenic. Green *et al.* found in their extensive study of temporal-lobe lesions in cats that the minority that showed aggressive behaviour had all had epileptic attacks, but also all of them had lesions that were more widespread into the hippocampal regions than with the non-aggressive animals, so that the different size and location of the lesions may account for the differences. I do not know of any convincing experiments showing positive behaviour disturbances related to on-going epileptic discharges in contrast to the negative effects of such discharges, with resultant disorganizations of behaviour and the emergence of simpler patterns, that are the result of the activity of those parts of the brain unaffected by the discharging lesion.

The human clinical material stresses three points that are little discussed by animal workers and may be very important. The first is the age of the subject affected by a lesion ; the second is other individual differences ; and the third point is the importance of the environment in which the subject is tested for the behaviour under question.

## Summary

I should like to try to summarize my general argument. In the first place, the brain-damaged child is handicapped as regards those functions, included under the general concept of intelligence, with which are bound up memory and learning. The term dementia

is usually applied to older subjects, and implies most typically a loss of recent memory—that is, the capacity to learn new material. Making allowances for the differences produced by age, the difficulty of the brain-damaged child in learning may not be fundamentally different. The poverty of our methods of localizing brain damage makes it impossible to implicate any particular area of the brain, and, in general, mental defect has been associated quantitatively with the amount of cortex damaged. However, the animal experiments make it possible that the deep temporal and mid-brain structures may be more important than others, but the powers of recuperation of the brain are very great.

Secondly, the psychological reaction of the child to being handicapped manifests itself in symptoms that are related to age, and understandable only when the emotional environment of the child is also taken into account. The brain-damaged-child syndrome does not exist in its own right, like an extensor plantar response; but only when the whole situation is considered can the contribution of the intrinsic handicap be assessed. The management of the brain-damaged child requires the fullest and deepest psychiatric approach.

Thirdly, the child who has epilepsy as well as brain damage has an additional handicap in two ways. Firstly, the epileptic activity may intensify the extent to which the brain damage interferes with cerebral activity, particularly when frequent attacks disrupt the activity of the normal parts of the brain. Secondly, the fits are a considerable social and emotional handicap, to which adjustment is difficult.

Epileptic children will long continue to be usefully studied psychiatrically for many reasons. For example, the interference with physiological functions during attacks can be much more carefully studied than can the non-epileptic effects of brain damage. On the other hand, the long-continued handicap of epilepsy imposes a strain on the family situation, the reactions to which illuminate many problems of parent–child relationship found in everyday child psychiatry.

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At a meeting of the court of the University of Leeds the Vice-Chancellor spoke about the practice, gaining ground in the new universities, of providing more broadly based courses each covering two of the traditional subjects of study. "It is thought possible," he said, "that courses of this kind, leading to 'honours' degrees, may well prove able in the coming years to hold their own in the matter of prestige, or even more than hold their own, with the older 'special honours' courses. It is perhaps too soon to tell. But there is increasingly wide recognition to-day both that knowledge does not entirely divide itself up without remainder into the traditional academic fractions, and also that many students will find themselves better educated for their future life and work if they do not confine their studies too rigidly to one specialist line of study. Emphasis is still placed upon study in depth; but the new courses will allow two subjects, each studied in the 'honours' manner, to be pursued to a high level of attainment."

# TWO CASES OF BENIGN STRICTURE OF OESOPHAGUS AFTER GASTRECTOMY FOR PYLORIC STENOSIS

BY

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It is known that benign oesophageal stricture may occur as a complication of upper abdominal surgery, particularly the surgery of peptic ulcer. Benedict (1960) reviewed 1,938 oesophagoscopies and reported nine cases of benign inflammatory stenosis after total gastrectomy for carcinoma of the stomach and 12 after surgery for duodenal ulcer (subtotal gastrectomy in 10, repair of perforation in two). In a miscellaneous group it occurred once each after pyloroplasty, proximal partial gastrectomy, oesophagectomy for oesophagitis and stenosis, partial gastrectomy for gastritis, revision of posterior gastro-enterostomy and vagotomy, and several other related procedures. He also noted one case after subtotal gastrectomy for pyloric obstruction, and one after first-stage gastrectomy for pyloric obstruction.

On reviewing the literature, very few accounts of benign stricture of the oesophagus after uncomplicated gastrectomy can be found in which the cardiac sphincter mechanism is left reasonably intact. Benedict's two cases have been mentioned. McKeown (1958) described two cases, and listed a similar case reported by Straus in 1950. A few more cases have been reported, but have usually followed upon severe post-operative problems such as distal loop obstruction. Within a period of one month recently, two such cases were seen in a surgical unit where a large number of gastrectomies are performed annually; such a case has not been encountered before. Such an event deserves comment and an effort to consider the aetiology.

## Case 1

A 40-year-old housewife first came for treatment on September 16, 1960, complaining of postprandial upper abdominal pain of five years' duration. It usually occurred about 30 minutes after eating and was relieved by alkali. For almost five years she had vomited a small amount at least once daily. Recently she had begun to notice retrosternal burning pain after vomiting. A barium-meal examination on September 23 showed gross pyloric stenosis but no evidence of oesophageal abnormality (Fig. 1). Laparotomy on October 5 confirmed the *x*-ray findings, and the cause was a duodenal ulcer on the anterior wall. A standard three-quarters anterior Polya–Hofmeister gastrectomy was performed. The post-operative course was excellent and she went home on the tenth day.

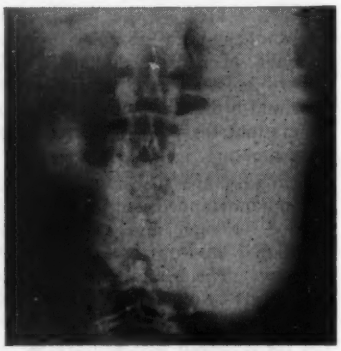

Fig. 1.—Case 1. Barium-meal radiograph, showing severe pyloric stenosis.

When first seen at follow-up clinic she stated that, almost immediately after leaving hospital, food began to stick high up in the gullet. This was thought to be functional and she was reassured. Five days later she was admitted as an emergency case, being unable to swallow even fluids. On November 22 a barium swallow revealed a simple stricture 5 in. (12.5 cm.) long and situated at the junction of the middle and lower third of the oesophagus (Fig. 2). Oesophagoscopy revealed much debris and inflammation of the upper oesophagus. Bougienage was unsuccessful, but two days later she swallowed a bougie herself (No. 8 English).

She has continued to pass bougies as an out-patient, gradually increasing the calibre up to No. 24 English. A histamine test meal on February 20, 1961, showed that she still had a very high total acidity and a normal free HCl. Recent *x*-ray examination showed some improvement in the stricture, and for the first time it was possible to demonstrate a hiatus hernia (Figs. 3 and 4).

## Case 2

A 50-year-old man employed at an automobile factory had a history of postprandial pain over a period of 18 months. The pain was mid-epigastric, and occasionally radiated through to the back. At no time had he vomited, and there was no retrosternal pain. A barium meal on October 3, 1960, revealed a gross pyloric stenosis possibly due to a pre-pyloric ulcer (Fig. 5). Shortly after, a standard threequarters anterior Polya–Hofmeister gastrectomy was

Fig. 2

Fig. 3

Fig. 4

Fig. 2.—Case 1. Barium swallow radiograph, showing a simple stricture of the oesophagus. Fig. 3.—Case 1. Barium swallow radiograph, showing the improvement after bougienage. Fig. 4.—Case 1. Barium-meal radiograph, revealing a hiatus hernia which may have been a sequel to the oesophageal stricture.

performed. His post-operative course was excellent, and he went home on the tenth day. A few days later he reported the rapid onset of severe dysphagia. A barium swallow revealed a benign stricture of the lower one-third of the oesophagus (Fig. 6). This was confirmed by oesophagoscopy, and bougienage was easily effected. He has continued self-bougienage, and very quickly gained 2 stone (12.7 kg.) in weight. A barium-meal examination in March, 1961 (Fig. 7), showed improvement in the stricture, but a hiatus hernia could not be demonstrated. Previous *x*-ray films had also failed to show this defect.

## Discussion

Both of these patients suffered from an equally severe pyloric stenosis. They were relatively young and fit, with no coincidental diseases. A four-day period of gastric lavage was carried out in each case, using Ryle's tubes. Identical operations were performed and the immediate post-operative course was excellent in each case, with removal of the tubes on the second day. In Case 1 a hiatus hernia could only be shown post-operatively, and in Case 2 this defect of the cardia has not been demonstrated despite careful search.

A review of the literature brings out the following factors important in the aetiology: incompetence of the cardia; pyloric obstruction and hypersecretion; suction tubes; and infection and thrombophlebitis from adjacent lesions.

### Incompetence of the Cardia

Allison (1948), in discussing peptic ulcer of the oesophagus, focused attention on the importance of the mechanism of the cardia in protecting the oesophagus from reflux. Besides describing the many factors that contribute to a competent cardia, he enumerated ways in which incompetence might develop: insertion of a rigid tube—for example, a Souttar tube through the cardia—surgical trauma, paralysis or lack of tone of the muscles as seen in very debilitated or flabby obese subjects, and, perhaps most important of all, the presence of a sliding mediastinal hernia of the cardia. These views are supported by many authors, and it is accepted that a sliding hiatus hernia is one of the commonest predisposing factors in oesophagitis. In Case 1 no hiatus hernia could be demonstrated until after the stricture was well established, while in Case 2 no hiatus hernia had ever been shown despite repeated investigations. It is possible that the defect in Case 1 may have been a sequel to the oesophageal stricture. It has also been shown (Rudstrom, 1954) that with hypersecretion in the stomach a regurgitation could develop, with subsequent changes in the oesophagus, even when the cardia was competent. He reported six cases of oesophageal stricture associated with duodenal ulcer, none of which had an associated hiatus hernia, and in support of his observations quoted Wangensteen and Leven's (1949) series of six similar cases.

### Pyloric Obstruction and Hypersecretion

In both cases pyloric stenosis was severe, but only in Case 1 was vomiting an important feature. Larson, Layne, and Howard (1942) observed the passive function of the oesophagus in vomiting, but cited the mechanical factors of rapid dilatation and excessive movement of the oesophagus leading to small fissures in the mucosa as being sufficient to cause ulceration. Pyloric stenosis is often encountered in reports of oesophageal stricture after upper abdominal surgery, and the obstructive vomiting must play an important part in the damage to the lower oesophagus. Rudstrom (1954) listed the ulcer disease, the hypersecretion, and the pyloric stenosis as the primary factors involved.

In Case 1 a post-operative histamine test meal showed a very high total acidity and a normal free HCl, so that pre-operatively there must have been marked hypersecretion. In Case 2 the post-operative histamine test meal showed a very low total acidity and no free HCl. It is possible that in the first case damage to the oesophagus due to the daily vomiting had been established before operation, and the early onset of a stricture was only coincident with or perhaps accelerated by pre- and post-operative suction tubes, and by any minor derangement of the cardia resulting from the gastrectomy. In Case 2 it is interesting to note that, besides the complete absence of vomiting throughout the history, the patient was almost achlorhydric as a result of his gastrectomy. Wangensteen and Leven (1949) felt that gastrectomy was the logical treatment for oesophageal stricture as it eliminated hypersecretion. Vomiting was not a factor in Case 2, and an adequate gastrectomy did nothing to prevent a serious stricture.

### Suction Tubes

Vinson (1941) stated that the use of tubes might contribute to oesophageal reflux by rendering the cardia

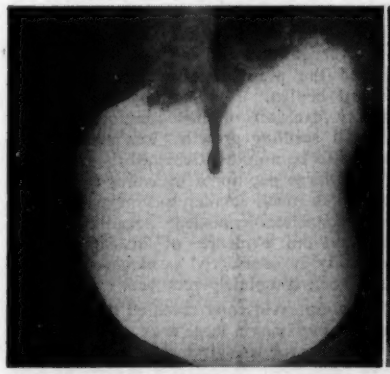

FIG. 5

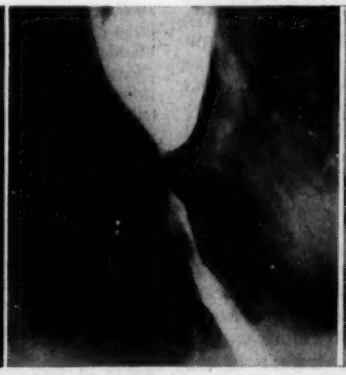

FIG. 6

FIG. 7

FIG. 5.—Case 2. Barium-meal radiograph, showing severe pyloric stenosis. FIG. 6.—Case 2. Barium swallow radiograph, showing a simple stricture of the oesophagus which occurred post-operatively as in Case 1. FIG. 7.—Case 2. Barium swallow radiograph, showing considerable improvement in the stricture after bougienage.

partially incompetent. Many other authors have reviewed the importance of suction tubes in causing damage to the oesophagus, and all seem to agree that it plays a minor part which may become more significant if oesophageal injury has already occurred. McKeown (1958) in reporting two similar cases made the interesting observation that after gastrectomy in each the Ryle tubes were left in only 72 hours, and strictures developed. He felt that they were the result of regurgitation of alkaline fluid through the Polya type stoma and hence into the oesophagus, and sought to prevent this by converting both to a Billroth type of anastomosis. After the second operation the tubes were left in for five days but the strictures disappeared.

The use of a Ryle tube was not thought to be an important factor here. It is conceivable that prolonged use of a tube could aggravate a pre-existing oesophagitis, but there was no proof of such disease, and use of the tube was very brief.

#### Infection and Thrombophlebitis from Adjacent Lesions

The relation between benign oesophageal stricture and coincident upper abdominal or thoracic lesions has never been clearly defined. Straus (1950) observed that most cases have in common the presence of a peptic ulcer, and the application of surgical trauma to the stomach or oesophagus. This trauma superimposed on chronic inflammatory disease of the upper abdomen might lead to retrograde thrombophlebitis in the lower oesophagus, and eventually to fibrosis and stricture. He felt that this could be explained anatomically in that the coronary vein drains blood from the stomach and receives tributaries from the lower oesophagus, and the lymphatics are closely allied. Allison (1948) observed that in reflux oesophagitis enlarged lymph nodes are always present around the lower end of the oesophagus, forming quite a large mass. He thought this might be a factor when the stricture is eccentric, especially in young children. Opposed to these theories is the fact that thrombosis cannot be shown microscopically, and also there may not be any coexistent inflammatory process. It is felt, therefore, that while these factors may be active in the pathogenesis, defects of the cardia and pyloric obstruction with vomiting are the most significant points in the aetiology.

Having considered several theories which have been brought forth to explain benign stricture of the oesophagus, it still remains that thousands of people have suffered from pyloric stenosis, but only a few have progressed to oesophageal stricture, with or without hiatus hernia and reflux. Larson *et al.* (1942) have suggested that regurgitation of gastric contents into the oesophagus is a normal process in a high percentage of cases. It appears, then, that other factors still unknown govern the response of the oesophagus to repeated exposure to acid gastric or alkaline jejunal contents.

#### Summary

Two cases are reported of benign stricture of the oesophagus following gastrectomy for pyloric stenosis. The rarity of this disease after uncomplicated gastrectomy is noted, and in reviewing the literature various aspects of the aetiology are assessed. Defects of the cardia and pyloric obstruction with hypersecretion are thought to be the most important factors, but other unknown forces may be involved.

I thank Mr. E. B. Whittingham for his advice and thoughful criticism in the preparation of this case report.

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## VESICAL HAEMORRHAGE AFTER MEGAVOLTAGE IRRADIATION

BY

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Since the availability of megavoltage therapy in this region an increasing proportion of cases of vesical neoplasm from my surgical practice have been referred for this type of treatment. In general the type of case chosen for megavoltage irradiation has been the extensive papillary or ulcerating tumour regarded as too large for either transvesical diathermy excision with radon-seed implantation or segmental resection, and therefore the treatment has usually been an alternative to total cystectomy. The results have been, in the main, eminently satisfactory, and it is thought that this type of therapy given for selected cases of vesical neoplasm represents a definite advance on previous methods, both surgical and radiotherapeutic.

Among 17 cases treated, however, were four instances of persistent and serious vesical haemorrhage which occurred after the irradiation and which resulted in problems of the utmost difficulty in relation to their surgical management.

It is proposed here to describe these four cases, briefly to consider the cause, to discuss more fully the methods used to control the haemorrhage, and, finally, to formulate some conclusions concerning the management of this complication.

### Case 1

A man aged 59 was first seen in hospital on December 14, 1957, because of painless haematuria. I.V.P. revealed a large papilliferous filling defect on the left lateral wall of the bladder, a small diverticulum, and normal pyelograms. Cystoscopy confirmed the presence of a large papillary tumour which looked benign. On January 10, 1958, a transvesical diathermy excision of this tumour, together with three other small seedling growths, was carried out. The tumours appeared to be non-invasive, and the histology was as follows: "The large papilloma measures 6 by 6 by 4.5 cm. There are three much smaller specimens. Histologically, they show considerable nuclear irregularity with numerous mitoses, but no evidence of invasion. The growths should probably be considered as carcinomata and they appear to have been completely removed."

In July, 1958, follow-up cystoscopy revealed the presence of multiple recurrences involving a large area of the bladder mucosa. Megavoltage therapy was given during the last two weeks of July. In November haematuria began; at first this was mild, but on January 7, 1959, the patient was readmitted with gross haematuria and a haemoglobin level of 37%. In spite of blood transfusions, "imferon,"

vitamin K, and bladder wash-outs, the bleeding persisted. Cystoscopy on January 27 revealed little except the impracticability of stopping the bleeding by transvesical diathermy—the bladder contained old blood clot which could not be evacuated even with a Bigelow evacuator, and a clear view was not obtained. Further cystoscopy after the instillation of "trypure" into the bladder was equally useless. Total cystectomy was considered, but the patient was in no way fit enough for such a major operation. It was decided to rely on further blood replacement, combined with bladder irrigations (0.05% chlorhexidine). On February 10 there was a sudden deterioration in the patient's general condition, and in spite of supportive measures he died soon after.

Necropsy revealed that death was caused by left ventricular failure due to cardiac infarction, and it was thought that this was probably aggravated by the long-continued haemorrhage from his carcinoma of the bladder. The bladder itself was full of blood clot, and there was a low sessile growth 3 cm. in diameter occupying the vault of the bladder, with smaller outlying tumours near the right ureteric orifice.

### Case 2

A man aged 54 was referred to hospital on July 18, 1958, because of painless haematuria. I.V.P. showed normal pyelograms, but there was a marked irregularity of bladder outline, suggesting an extensive neoplasm. Cystoscopy confirmed the presence of a large sessile neoplasm involving the whole of the left side of the bladder and extending well into the vault. Initial treatment was by megavoltage therapy, which was given in August. In December haematuria began. Cystoscopy on January 2, 1959, showed the neoplasm to be still present but regressing. The site of the haematuria could not be determined, although a clear view was obtained, and it persisted unremittingly in spite of bladder wash-outs with trypure, $AgNO_3$, and chlorhexidine. Further cystoscopy on January 29 showed definite regression in the size of the tumour, but the haematuria continued. Vitamin K and calcium gluconate were prescribed. The Hb level remained around 70% without transfusion, and the patient was therefore allowed home and kept under observation as an out-patient.

During most of the year 1959 he continued with mild to moderate haematuria, but his Hb level never dropped below 50%. On January 22, 1960, cystoscopy revealed that the main growth had completely disappeared, but there was a recurrence surrounding the internal urinary meatus. A biopsy report stated: "A small segment of inflamed transitional-celled tumour of the bladder, which is rapidly growing but well differentiated. No evidence of invasion in this piece." Total cystectomy was advised and carried out on February 16, the ureters being transplanted into the colon. No special difficulty which could be attributed to the previous irradiation was noted during the cystectomy. The abdomen had to be reopened on February 22 because of small-gut obstruction due to adhesions, but after this he made an excellent recovery and was discharged home on March 12. The removed bladder showed no sign of the original invasive tumour, but there was a ring of sessile growth surrounding the internal urinary meatus and spreading on to the right side. Microscopically it was an undifferentiated carcinoma. Since discharge he has remained well apart from failure to regain his pre-operative weight and energy. Chest *x*-ray films, however, in January, 1961, revealed two small secondary deposits in the upper lobe of the right lung. He was seen by a thoracic surgeon (Mr. F. R. Edwards), who advised lobectomy on the grounds that these were isolated metastases; but the patient refused further surgery.

He had a mild electrolyte disturbance in February, which responded to intravenous sodium lactate and tube drainage of the rectum. When last seen (October, 1961) he was quite well in spite of the chest secondaries, and the electrolytes were normal.

### Case 3

A man aged 47 was referred to hospital on October 7, 1958, because of painless haematuria. I.V.P. showed a large papilliferous filling defect on the left side of the bladder and normal pyelograms. Cystoscopy confirmed the presence of a very large papillary neoplasm involving the whole of the left wall and vault and extending down on to the trigone. Bimanual examination revealed no induration of the bladder base. A biopsy was taken and the report was "transitional-celled papilloma."

Megavoltage therapy was given in November. Cystoscopy on May 9, 1959, showed that the main tumour had completely disappeared. There was a small amount of residual tumour on the left side and on the roof of the bladder, which was regressing.

On June 21 he was readmitted with haematuria and a Hb of 70%. Vesical drainage via an indwelling Foley catheter was instituted and the bladder was washed out with 0.05% chlorhexidine and "trypure novo." The haemorrhage continued and blood was transfused. This conservative regime was followed for the next six weeks, but the haematuria never lessened. Over 20 pints (11.4 litres) of blood were given during this period, and on August 11 his Hb was 30% and it was obvious that he would die if the bleeding was not stopped. The same day both internal iliac arteries were ligated. It was felt, however, unsafe to rely on this alone, so after extraperitoneal ligation of these vessels the bladder was opened. A very small residual area of tumour was found situated above the right ureteric orifice, from which blood was slowly seeping. The whole area was excised with a diathermy loop and the bladder closed. This combined operation stopped the vesical haemorrhage, and undoubtedly saved the patient's life. Histology of the removed specimen was reported on as follows: "An unfixed piece of necrotic tissue showing some calcification around the edge." By September 12 his Hb was 77%, and further blood transfusion had not been required since the operation. The suprapubic wound did not heal, however, and it was resutured on October 23.

On November 9 haematuria recurred, but this was only a mild episode and soon ceased. He was discharged home on December 21 with his suprapubic wound healed, micturating normally, and with no haematuria.

He was readmitted, however, on January 1, 1960, with further haematuria, once again severe. Three pints (1.7 litres) of blood were transfused and the patient was prepared for possible total cystectomy. On account of the previous findings of a near-normal bladder it was decided to open the bladder first to make sure the operation was essential. Owing to previous experience, due to blood clot and poor vision, cystoscopic assessment was considered unreliable. This operation was done on January 22. The bladder appeared normal apart from a small papillomatous area situated on the left side of the bladder away from the previous area of diathermy resection. This small area, not larger than a millet seed, was bleeding continuously. The area was excised with the diathermy loop, cutting deeply, and the bladder closed, drainage being effected by an indwelling Foley catheter passed per urethram. There has since been no further haemorrhage. The suprapubic wound healed and the patient was discharged on February 10, 1960. The removed specimen, however, is reported histologically as transition-celled carcinoma of the bladder. The patient is having regular follow-up cystoscopies at three-monthly intervals. When last examined, in July, 1961, the bladder was quite clear, with no evidence of recurrence of the neoplasm, and there had still been no recurrence of the haemorrhage.

### Case 4

A man aged 64 was referred to hospital on August 27, 1958, with painless haematuria. He had been under treatment for pulmonary tuberculosis for several months with

satisfactory progress, but the haematuria had caused his Hb to drop to 34% ; at that time he refused to enter hospital. An I.V.P. showed no evidence of tuberculosis of the urinary tract, both pyelograms being normal, but there was a large basal filling defect in the bladder. Clinically the prostate was not enlarged. Urine culture for tubercle bacilli was negative. At this time he refused cystoscopy, but later agreed, and an examination was done on November 27 after transfusion of several pints of blood. The findings were a very extensive papillary neoplasm with short thick fronds and a sessile base covering both the right and the left walls of the bladder and extending towards the internal meatus. Bimanual examination revealed no palpable induration. A biopsy was taken and the report was as follows: "Section shows a simple papilloma with no obvious malignancy, although the amount of tissue present is small." The tumour was regarded as probably malignant in spite of this report, but not infiltrating deeply. Megavoltage therapy was advised and given in December.

Slight haematuria recurred on May 7, 1959, and cystoscopy revealed an excellent result from the irradiation, the right and left walls of the bladder being quite clear of growth. There were, however, two small papillary areas remaining on the bladder base which were regressing. He remained well until August, when further haematuria recurred and persisted. Perurethral fulguration of the bleeding area was attempted, with no success. Bladder irrigations with 0.05% chlorhexidine, $AgNO_3$, and trypure were also ineffective. Blood transfusion became necessary and had to be repeated; further, it became obvious that direct surgery would have to be undertaken. On October 1 the bladder was opened; a large blood clot was removed, and a small papillary area about 1 cm. in diameter lateral to the left ureteric orifice was found to be the source of the bleeding; this was excised deeply with the diathermy loop. The remainder of the bladder appeared normal, and, as the bleeding was controlled, the bladder was closed. The patient recovered quickly from this operation, the urine remained crystal-clear, and he was discharged on October 15.

Haematuria recurred, however, on November 16, and continued unremittingly. Once again bladder irrigations and instillations were of no avail. Many pints of blood were transfused during the next six weeks, and cystoscopy showed the bleeding-point to be a very small area situated at the site of the previous diathermy excision. Perurethral fulguration was applied. This controlled the bleeding for three weeks, after which it recurred and persisted. On January 20, 1960, after further blood transfusions, both internal iliac arteries were ligated via an extraperitoneal approach. This had very little effect on the haematuria, which continued, and a further 5 pints (2.8 litres) of blood had to be transfused. On February 11 the bladder was reopened and found to be quite clear of neoplasm. Just lateral to the left ureteric orifice there was a deeply ulcerated area about the size of a large pinhead, which was bleeding freely. The bladder wall surrounding this area was thickened, and it was again possible to excise the area deeply with the diathermy loop. The bladder was closed completely and drained via an indwelling Foley catheter. His wound healed rapidly, and he was discharged on March 2.

On June 28, however, he was readmitted with yet further haematuria, and 2 pints (1.1 litres) of blood were transfused. On cystoscopy, the blood clot was evacuated and the bladder appeared normal. The site of haemorrhage could not be seen. On July 4 the Hb had dropped to 30%, and 3 pints (1.7 litres) of blood were transfused. On further cystoscopy more blood clot was evacuated. On this occasion the bleeding-point was seen above the left ureteric orifice and diathermy was applied. On July 18 he was still bleeding heavily. After further transfusion his bladder was reopened for the third time on July 21, and a small papillary recurrence just above the left ureteric orifice was deeply excised with the diathermy loop, and the edges of the resulting defect were sutured. The bladder was again completely closed and drained by an indwelling Foley catheter. By August 3 the wound had completely healed, his urine was crystal-clear, his Hb 85%, N.P.N. 26 mg./100 ml., and he was again discharged. The histological report on the specimen removed on July 21 stated: "The tumour is a sessile, papillary tumour of transitional epithelium. No invasion is seen, but mitotic figures and abnormal nuclei are so numerous that there is little doubt that the tumour is malignant." In view of this report it was decided to carry out total cystectomy if further haemorrhage occurred, or if cystoscopy at regular intervals showed any sign of recurrence.

He bled again in January, 1961. A further I.V.P. showed normal pyelographic appearances, and after being prepared for total cystectomy his bladder was reopened on January 5 to assess the local condition prior to performing this operation. Apart from blood clot the only abnormality was a small area of heaped-up epithelium about 0.5 cm. in diameter situated above the left ureteric orifice. It was decided not to do a total cystectomy, and once again a transvesical excision of the bleeding area was performed. On this occasion the histology was as follows: "In paraffin section the appearances are those of a simple papilloma. There is no evident malignant change." Even after this fourth transvesical operation his wound healed quickly, and he was discharged on February 2.

Once again, however, success was only short-lived. He began bleeding again on April 12 and his Hb started to drop. He was transfused and total cystectomy performed on April 28, the ureters being transplanted into the colon. The operation was technically more difficult than usual because of the previous interventions, but nevertheless the patient made an excellent recovery and was discharged home on May 31.

Macroscopically, the removed bladder looked almost normal. The histological report was as follows: "Microscopically there is well-marked cystitis, but neither tumour nor necrosis can be recognized in five paraffin sections from different parts of the bladder. In places the muscle is almost entirely fibrous and contains macrophages and some foreign-body giant cells. In such areas there are a few cells that cannot be identified but which do not seem to be tumour cells."

### Irradiation Dosage

The total dose and rate of irradiation given to these four cases was as follows. *Case 1*: 5,090 rads maximum and 4,920 rads minimum in 15 treatments over 21 days. *Case 2*: 5,100 rads maximum and 4,700 rads minimum in 15 treatments over 21 days. *Case 3*: 5,500 rads maximum and 5,000 rads minimum in 15 treatments over 18 days. *Case 4*: 5,500 rads maximum and 5,000 rads minimum in 15 treatments over 22 days.

### Discussion

The cause of persistent and severe vesical haemorrhage after megavoltage therapy is to a large extent speculative. There is, however, some evidence that irradiation causes damage to the vesical blood-vessels. Wallace (1954) describes a "necrotizing arteriolitis" as one of the ill-effects of irradiation on the bladder. In this condition the muscle coat of the arterioles is replaced by fibrous tissue and the normal contractility of the arterioles is consequently impaired.

In 1959 Wallace, together with N. R. Mackay and D. W. Smithers, gave the opinion that as a consequence of heavy irradiation the bladder mucosa becomes thin, blanched, atrophic, and inelastic, while the submucosa shows marked fibrosis, tending to split readily and cause persistent bleeding from previously damaged submucosal vessels.

Riches and Windeyer (1960), describing 11 cases of severe vesical bleeding among 91 patients treated by megavoltage therapy, state that in the majority the bleeding came from extensive telangiectases, but in others there was destruction of the mucous membrane, leaving a shaggy hyperaemic surface from which a continuous ooze occurred.

Such telangiectases or shaggy hyperaemic surfaces have not been observed in these four cases, nor has any evidence of necrotizing arteriolitis been found even after re-examination of all the pathological specimens available. In the four cases described here it would appear that the persistent and recurrent haemorrhage has occurred from areas of residual or recurrent tumour formation. The only possible exception to this was the finding of a very circumscribed but deeply ulcerated area causing the bleeding at the second transvesical operation in Case 4. This could conceivably have been due to necrotizing arteriolitis, but unfortunately the specimen was too severely damaged by diathermy for histological examination to be helpful.

It is of course a clinical fact that vesical neoplasms which have not been subjected to irradiation seldom bleed in such a serious and persistent manner. It is difficult to escape the conclusion, therefore, that vesical irradiation can occasionally, by the production of either necrotizing arteriolitis or some other lesion so far undiscovered, so alter the arterioles or capillaries carrying blood to recurrent or residual tumour areas as to allow them to rupture spontaneously and to bleed seriously and unremittingly.

## Treatment

When persistent haematuria follows megavoltage therapy the following methods of treatment are available: (1) conservative—that is, bladder wash-outs, haematinics, blood transfusion, vitamin K, etc.; (2) cystoscopic diathermy to the bleeding area; (3) a transvesical attack with diathermy excision of the affected part of the bladder; (4) ligation of the internal iliac vessels; (5) urinary diversion without total cystectomy; and (6) total cystectomy.

*Conservative Therapy.*—In all cases this has been the first choice of treatment, owing to the fact that in no case was the patient's general condition at all serious to begin with. The immediate treatment has been to insert an indwelling Foley catheter and to wash out the bladder frequently with 0.05% chlorhexidine solution. When the Hb level had dropped below 60%, blood transfusions were given. Attempts were made to disperse intravesical clot with trypure novo solution (pure crystalline trypsin stabilized by the addition of 50 mg. of an inert calcium salt dissolved in 100 ml. of sterile saline). In all cases the object was to get the bladder clear of clot and haemorrhage so that an accurate assessment of the cause of the bleeding could be made at cystoscopy. This objective was seldom attained, and it must be accepted that cystoscopy is often inaccurate in this condition because either of retained blood clot or persistent bleeding. Furthermore, Case 1 has shown that conservative therapy can be persisted with too long.

*Cystoscopic Diathermy to Bleeding Area.*—This was attempted in Case 4 on two occasions. The first was quite unsuccessful, and on the second occasion the bleeding was controlled for about three weeks. In the other cases massive blood clot and poor vision rendered this method of controlling the haemorrhage quite impracticable. It is my opinion that cystoscopic diathermy is seldom a practical proposition in these cases. The affected bladder invariably contains blood clot which is difficult to evacuate completely, and in only one of the cases has it been possible to obtain good enough vision to apply the electrode with any degree of precision. In addition it seems doubtful whether it might be effective except in very mild cases. This opinion is supported by the experience of Riches and Windeyer (1960), who state that light diathermy sometimes makes the bleeding worse and deep diathermy may stop it for a time but increases the area of necrosis.

*Transvesical Diathermy Excision of Bleeding Area.*—This appears to have been a highly effective method for immediate control of the haemorrhage. Unfortunately, however, the success of this method did not usually prove permanent. In Case 4 the operation was carried out four times and eventually had to be followed by total cystectomy. In Case 3 this method was used on two occasions. The first time the bleeding was controlled for five months, and for the 21 months after the second operation there had been no recurrence of bleeding or tumour formation. In both these cases the internal iliac vessels were also ligated. It is difficult to know how much this contributed to the measure of success achieved by the transvesical diathermy excision, but it is my opinion that the arterial ligation made little or no difference.

*Ligation of Internal Iliac Vessels.*—Schmitt (1953) first proposed this method for vesical haemorrhage and described four cases in which the haemorrhage occurred after prostatectomy. Stapor and Majurek (1957) recommended the ligation as a palliative measure in severe vesical haemorrhage due to inoperable carcinoma of the bladder and described six successful cases. In the above four cases the operation was first used in Case 3, when the patient was severely exsanguinated. It was combined with transvesical excision of the residual neoplastic area with a diathermy loop, and undoubtedly the combined operation was successful. Whether the arterial ligation if performed alone would have been effective or, alternatively, whether the transvesical excision if performed alone would have been effective, is a matter of conjecture. In spite of the ligation the haemorrhage recurred in this case, however, and a further transvesical operation was required before the patient finally recovered. In Case 4 the arterial ligation was unsuccessful and transvesical diathermy excision had to be carried out on three occasions after this, and eventually total cystectomy was required. In each case the operation has been extraperitoneal ligation of both internal iliac vessels close to their origins from the common iliacs. No attempt has been made to place the ligature on the anterior division and no untoward sequelae have occurred.

*Urinary Diversion without Total Cystectomy.*—I have not used this method. Riches and Windeyer (1960) diverted the urine into an iliac loop in three cases but failed to stop the bleeding, and total cystectomy was required. In a fourth case diversion was combined with ligation of both internal iliac arteries and segmental cystectomy, but even after this bleeding recurred. It would therefore appear that urinary diversion alone is not sufficient to control the haemorrhage. In addition, it seems undesirable to leave a defunctioned bladder

which has been affected by diffuse neoplastic growth even if at the time the growth does appear to have been eradicated.

*Total Cystectomy.*—Case 2 was treated by this method, the ureters being transplanted into the colon. The removed bladder showed new tumour deposits of undifferentiated carcinoma surrounding the internal meatus. Obviously no lesser operation would have sufficed in this case. Case 4 was also treated by total cystectomy, but only after four operations of transvesical excision and one of extraperitoneal ligation of the internal iliac vessels. The removed bladder showed no histological evidence of residual tumour or of radionecrosis, but the operation had become necessary because of repeated haemorrhage in spite of temporary control by less radical methods.

The prolonged hospitalization and the number of surgical interventions required in these cases illustrate the extreme gravity of anything other than mild haemorrhage after megavoltage therapy. It is not surprising that most surgeons resort to total cystectomy, and this was the treatment required for two of the four cases. It would also appear that total cystectomy would have been the only satisfactory method of controlling the fatal case (Case 1) had the myocardial infarction not occurred, as the necropsy showed multifocal recurrences in the bladder. It may well be that Case 3 would also have been better treated by this method, and certainly for the patient himself the ordeal would have been no greater. One very severe operation may well be preferred to several less major interventions. On the other hand, however, it may fairly be said that the less radical treatment has left him better off than he would have been if total cystectomy had been chosen. He has not bled for over 21 months, and follow-up cystectomy has shown no evidence of recurrence of the tumour and he retains the normal and physiological method of micturition.

Both Cases 3 and 4 illustrate the fact that transvesical excision of the bleeding area can be relied on to control the bleeding for several weeks, if not indefinitely. This is important because it means that total cystectomy need never be resorted to in an exsanguinated or weakened patient. The lesser operation should be chosen first, and, if considered necessary, total cystectomy should be proceeded with when the patient has fully recovered from the effects of the haemorrhage.

## Management

With regard to the management of these difficult cases, my experience supports the current surgical opinion that severe and persistent haemorrhage after megavoltage therapy will usually require total cystectomy. Before resorting to this operation, however, a reasonable period of conservative treatment should be given a trial and cystoscopy may well show that the neoplasm has been almost completely eradicated by the irradiation. In many cases, however, extensive blood clot will render cystoscopy a very inaccurate and fruitless procedure. Attempts at clot dispersal with enzyme solutions and a Bigelow evacuator are very likely to fail, and if tried should not be persisted with.

In all cases it may well be worth while opening the bladder and carrying out a transvesical excision of the bleeding area before resorting to total cystectomy. The bleeding-point will often be found to be a small recurrent neoplastic area and the main tumour may well have completely or almost completely disappeared. This relatively minor operation can be carried out on a patient who is considerably weakened by loss of blood, and, although permanent success seems unlikely, the bleeding will be controlled for several weeks, during which time the patient's Hb level can be rectified at leisure. If, after this, further bleeding recurs it is probably best to proceed with total cystectomy, but this operation should not be performed on a weakened and exsanguinated patient. If necessary a second transvesical excision to regain control of the haemorrhage followed by total cystectomy in 8 to 10 weeks' time is recommended. However, the temptation to persist with lesser operations on account of non-malignancy and very small areas of recurrence as a cause of the bleeding should probably be resisted in most cases.

## Summary and Conclusions

Four cases of persistent haemorrhage occurring after megavoltage irradiation for extensive vesical neoplasm are described. This complication after megavoltage therapy is regarded as an extremely serious condition; if it is not controlled by conservative measures within two to three weeks, total cystectomy should be seriously considered, even if cystoscopy shows that the original tumour has almost completely disappeared. Cystoscopic diathermy has not proved practicable, and ligation of the internal iliac arteries is not effective. The bleeding, however, can usually be controlled by transvesical diathermy excision of the bleeding area, and this operation alone, possibly repeated, may suffice in some cases. In others it can be a useful preliminary to total cystectomy, allowing the patient to recover fully from his blood loss.

I am grateful to Dr. M. A. Stewart for providing the irradiation details, and to Mr. J. Humphries, my registrar at the time, for suggesting the internal-iliac-arterial ligation in Case 2. I also thank the nursing staff at Broadgreen and Newsham General Hospitals for their devoted and skilful care of these seriously ill patients.

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At the opening meeting of the Manchester Medical Society Dr. J. F. WILKINSON described his recent tour of Japan and Thailand and discussed the facilities for medical teaching and research in the two countries. He described the Eighth Congress of the International Haematological Society in Tokyo, and gave an account of his tour of other Japanese medical centres, including the cities of Hiroshima and Nagasaki. In Thailand active medical research work was being carried out, though under less easy conditions than in Japan. There was an abundance of interesting clinical material, particularly of a haematological character. There were many cases of chloramphenicol-induced aplastic anaemia and thrombocytopenic purpura, as well as leukaemias, haemolytic anaemias, and haemoglobinopathies, which offered great scope for further clinical and haematological research.

# BLOOD LOSS DURING SURGERY

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The introduction of blood transfusion marked a milestone in the progress of surgery comparable to the discoveries of anaesthesia and of measures to combat surgical infections. Blood transfusion, however, introduces certain hazards of its own, and there is by no means uniformity of opinion among surgeons on the indications for blood transfusion in surgical operations.

There can be little doubt that blood loss requiring transfusion should be anticipated before the body's ability to compensate for it fails and hypotension develops. Less blood is required to prevent such hypotension than to correct it (Reeve, 1961, unpublished data), and it is widely known that even short periods of hypotension can produce irreversible sequelae in patients with vascular disease (Shackman *et al.*, 1960). Maintenance of normal blood-pressure and blood-volume is the keynote of successful surgery, particularly in the elderly and neonatal patient.

When severe blood loss leaves no doubt about the need for transfusion, a further hazard seen with increasing frequency is that of excessive transfusion, which is also poorly tolerated in the elderly patient or in the presence of cardiac disease.

In assessing the need for transfusion three courses are open to the surgeon. He can wait until signs of shock appear before giving blood. This policy undoubtedly avoids some unnecessary blood transfusions but courts disaster in the vulnerable patient, especially in the post-operative period, when the onset of shock may be recognized too late. It is also disadvantageous because a depleted blood-volume, although insufficient to produce shock, may still increase morbidity, delay wound-healing, and prolong convalescence.

A second policy is to give blood routinely for major operations usually requiring transfusion. This policy still results in some unnecessary transfusions. Also when massive bleeding occurs the surgeon has to depend upon clinical judgment alone to determine the volume of blood required, with the resulting risks of inadequate or excessive replacement.

The third and obviously ideal course is to use a reliable method of measuring blood loss as it occurs, so that accurate blood replacement can be effected. This paper describes our experience with a simple sponge-weighing technique to measure operative blood loss and some of the lessons learned from adopting this policy.

*Material.*—Data are presented from a total of 412 cases in which blood loss was measured gravimetrically. The operations involved were 255 cases of thyroidectomy and neck surgery, and 52 vascular, 48 abdominal, 28 urological, and 29 breast operations (Fig. 1).

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## Method of Estimation of Blood Loss

Simple scales accurate to 5 g. and containing an adequate-sized pan were used (Fig. 2). The difference in weight between each blood-stained sponge and the average weight of a dry one of similar size is recorded in grammes and is taken to represent millilitres of blood lost. Some additional allowance is made for blood on gowns and large drapes and other sites if these cannot be weighed. This additional blood should be minimal if care is taken with swabbing and if oiled-silk under-sheets are used. Dry swabs and sponges were used throughout all cases.

Only known volumes of water are run through the suction line, and the sucker bottle is accurately calibrated and the contents are measured. In many cases blood volume was measured immediately after operation, using red cells tagged with $^{51}Cr$ (Reeve *et al.*, 1959). Thus the accuracy of measured blood losses (and replacement) was checked.

## Results

The results of the 412 measurements are shown in Fig. 1. The range of bleeding is noteworthy. The magnitude of the blood loss in several standard procedures is impressive. In radical mastectomy the variation in blood loss was considerable, extending from 380 to 3,200 ml. During subtotal gastrectomy the range was from 200 to 1,800 ml. and during prostatectomy 150 to 2,750 ml.

The extent of haemorrhage beyond a limited range cannot be estimated reliably by "experience." In long operations especially, or when the blood loss is severe, estimations of blood loss may be wildly misleading.

It is interesting that an awareness of bleeding and a systematic measurement of it seems to have resulted in a progressive reduction in blood loss during these operations. In three types of operations—total thyroid lobectomy, thyroidectomy for intrathoracic goitre, and bilateral subtotal thyroidectomy—there has been a reduction in the average blood loss each year. Greater care is exercised by the surgeon, who is kept continually conscious of blood loss.

As stated, the accuracy of replacement during excessive haemorhage can be checked post-operatively by determining the patient's blood volume.

A man aged 68 was admitted suffering from a ruptured abdominal aneurysm. During an operation for resection of the aneurysm and its replacement by a prosthetic graft the measured blood loss was 15 litres, and this volume of fresh blood was given by two simultaneous transfusions through large-bore cannulae. On checking his post-operative blood-volume it was found to be 4,393 ml. with a red-cell mass of 1,882 ml., which are well within the normal range; at the end of the operation his condition was satisfactory and his blood-pressure was well maintained.

## Discussion

We would deprecate an attempt to establish figures for average blood loss during particular operations, for such average figures may well give surgeons and anaesthetists a false sense of security. For example, in an operation such as thyroidectomy our average blood loss is only 250 ml., but in a number of instances the

loss was well over 1 litre. In operations such as radical mastectomy, prostatectomy, or abdomino-perineal resection, the surgeon and anaesthetist should employ some technique for measuring blood loss, otherwise accurate replacement cannot be achieved.

On many occasions we have measured the patient's blood-volume before and after operation, using red cells tagged with $^{51}Cr$, and have found that the blood replacement was accurate even after a large operative blood loss, thus confirming the validity of the simple method of measurement here described. In cases of massive haemorrhage we submit that it is impossible safely to give large volumes of blood without accurate knowledge of the amount of blood lost.

In our own experience, where we have attempted to guess the blood loss we have made errors of up to 100%. The difficulty of estimating losses accurately is accentuated when the losses are great or when the operating-time is prolonged. The simple gravimetric technique described here gives no extra work to the theatre staff and has been shown to compare favourably with other methods, such as weighing the patient or

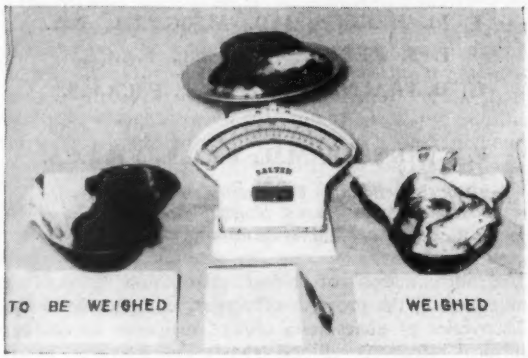


FIG. 2.—Scales used for measuring blood loss.

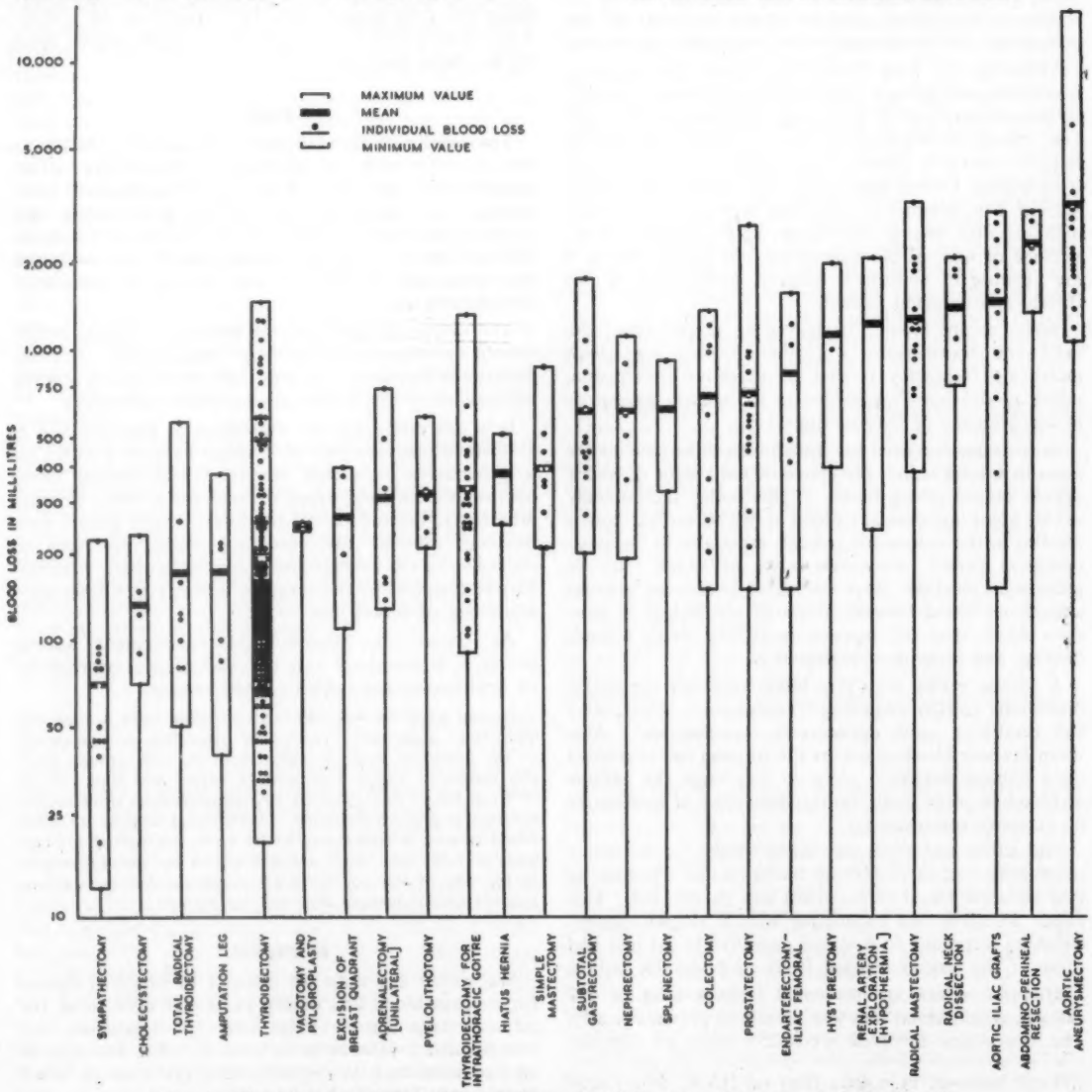


FIG. 1.—Blood loss recorded at 412 operations, plotted for convenience on a logarithmic scale.

colorimetric determination of operative bleeding (Baronofsky *et al.*, 1946). Moreover, sponge-weighing and constant reference to the volume of blood in the suction bottles enables progress assessments of blood loss to be made and blood replacement to be geared accurately to the loss.

Routine use of this method improves the surgeon's judgment of the volume of blood being lost. A better surgical technique is likely to be developed as a result of increased attention to measurement of the blood loss.

Blood is a valuable commodity. Accurate measurement of blood loss leads to saving of blood for our community's blood banks. In some patients undergoing major operations the measured blood loss is small and transfusion is clearly unnecessary.

With this simple method geriatric patients can usually be maintained at a normotensive level even during such radical surgery as aortic replacement. Survival rates show gratifying improvement. In view of its many advantages, this simple method should be a routine part of modern theatre practice.


### Summary

A simple gravimetric method for measuring loss of blood during surgery has been discussed.

This method allows of the rational replacement of blood lost and minimizes the risk of over- or under-transfusion.

The use of this procedure is recommended during all major surgical operations.


We are grateful to Mr. G. Logan and Miss M. Simpson for preparation of the illustrations.


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# BROW PRESENTATION

BY


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Brow presentation is associated with high mortality and morbidity of both mother and foetus. That it is the rarest of all malpresentations only increases its importance in obstetric practice, for few obstetricians are able to gain sufficient experience of the condition. Many of the papers published show combined statistics of face and brow presentations and deal with series of cases encountered over many years. In this paper 35 consecutive cases of brow presentation that occurred in Chittaranjan Seva Sadan College between April, 1953, and January, 1961, have been analysed in an attempt to show the recent trends in the management of this serious condition.

*Incidence.*—During the period of review there were 60,130 deliveries, giving an incidence of brow presentation of 1:1,718. The figures reported by different authors varied from 1:667 (Moore and Dennen, 1955) to 1:3,453 (Posner and Buch, 1943). The average incidence was found to be 1:1,804 (Table I).

TABLE I.—*Incidence and Foetal Mortality*

| Authors | Years of Survey | No. of Deliveries | No. of Brow Cases | Incidence | Foetal Mortality |
|---|---|---|---|---|---|
| Hellman *et al.* (1950) | 1896–1948 | 65,930 | 44 | 1 : 1,498 | 25% |
| Kenwick (1953) | 1930–1952 | 76,062 | 26 | 1 : 2,941 | 8·7% |
| Madden (1956) | 1945–1955 | 13,774 | 13 | 1 : 1,059 | — |
| Magid and Gillespie (1957) | 1945–1955 | 39,371 | 16 | 1 : 2,473 | 6·25% |
| Moore and Dennen (1955) | 1931–1953 | 24,030 | 36 | 1 : 667 | 8·3% |
| Morris (1953) | 1934–1950 | 64,817 | 53 | 1 : 1,224 | 28·3%* |
| Posner and Buch (1943) | 1914–1942 | 46,058 | 13 | 1 : 3,453 | 20% |
| Posner *et al.* (1957) | 1943–1956 | 50,345 | 23 | 1 : 2,189 | 6·3%† |
| Simpson (1950) | 1935–1949 | 31,534 | 38 | 1 : 829 | 13·1% |
| Skalley and Kramer (1960) | 1953–1958 | 63,104 | 27 | 1 : 2,337 | 7·7% |
| Tancer and Rosanelli (1957) | 1935–1957 | 27,937 | 22 | 1 : 1,269 | — |
| Present series | April, 1953, to January, 1961 | 60,130 | 35 | 1 : 1,718 | 8·5% 25·7%* |
| Combined Series | | 563,092 | 346 | 1 : 1,804 | |

* Uncorrected. †Face and brow.

## Aetiological Factors

Many maternal and foetal factors have been said to be the cause of brow presentation. Tancer and Rosanelli (1957), however, failed to discover any important maternal predisposing factor. White (1954) found no cause in 33 out of 100 collected cases. He concluded that most of the brow and face presentations, if not all, were primary in nature and were due to the increased tone of the extensor muscles of the neck of the foetus. Excluding multiparity, no cause was detected in 14 cases (40%) of the present series.

*Contracted Pelvis.*—According to MacLennan *et al.* (1955) brow presentation is nearly always associated with contracted pelvis. Greenhill (1955) mentioned that it occurred in 53.8% of the cases reported by Hellman *et al.* (1950). Simpson (1950) found the incidence to be 23.7%, whereas Madden (1956) had only one contracted pelvis in 33 cases. In the present series contracted pelvis was noted in 17.1% of cases—a figure in close agreement with those of Kenwick (1953) and Morris (1953) (see Table II).

TABLE II.—*Aetiological Factors (Percentages)*

| Authors | Primiparae | Multiparae | Contracted Pelvis | Big Baby (>8 lb.) | Prematurity |
|---|---|---|---|---|---|
| Hellman *et al.* (1950) | 37·2 | 62·8 | 53·8 | — | Nil |
| Kenwick (1953)* | 33·3 | 66·7 | 15·1 | 10·9† | 12·4 |
| Madden (1956) | 55·5 | 44·5 | 7·7 | 30·7 | Nil |
| Morris (1953) | 62·2 | 37·8 | 15·1 | 31·3 | 15·1 |
| Simpson (1950) | — | — | 23·7 | 13·1 | 8 |
| Skalley and Kramer (1960) | 22 | 78 | 11 | 15 | 18·5 |
| Present series .. | 40 | 60 | 17·1 | 11·4 | 28·5 |

* Combined figure of face and brow.
† Birth weight 8 lb. 8 oz. (3,858 g.) or above.

*Parity.*—Hellman *et al.* (1950) observed that 62.8% of their brow presentations occurred in multiparae, in contrast to the average clinic figures of 52.9%. But Morris (1953) and Madden (1956) found 62.2% and 55.5% of their cases respectively to be in primiparae. Out of 35 cases in the present series, 14 (40%) were in

primiparae and 21 (60%) in multiparae. During the period of survey 16,327 primiparae and 43,803 multiparae were confined, with a brow incidence of 1:1,166 and 1:2,086 respectively—brow presentation thus occurring much more often in primiparae.

*Prematurity.*—The infants weighed 5 lb. 8 oz. (2,495 g.) or less in 28.5% of cases—a figure much below the average hospital figure of 40%. This confirms the findings of Hellman *et al.* (1950) and Madden (1956), who had no premature infants in their series, although Skalley and Kramer (1960) noted a higher prematurity rate in brow cases than in their general obstetric population. Kenwick (1953) and Posner *et al.* (1957), giving combined statistics of face and brow presentations, found prematurity in 12.4% and 25% of their cases respectively.

*Big Baby.*—While the part played by small infants in the aetiology of brow presentation is controversial, almost all authors have found an increased association of large infants with this condition. In this series eight infants (22.8%) weighed more than 7 lb. (3,175 g.), the corresponding average hospital figure being 9%. In four of these eight infants the birth weight was more than 8 lb. (3,630 g.).

*Other Factors.*—Analysis of cases by age-group did not show any significant difference from the general pattern of all confinement cases. In one case of compound presentation the vertex was converted to brow during replacement of the prolapsed foot. Foetal ascites was present in one case. Other aetiological factors, such as cord round the neck and multiple pregnancy, were not found.

## Diagnosis and Positions

As in all other published series, in most of these cases the diagnosis was made very late in labour. In fact, in two cases it was not made until they were admitted with ruptured uterus.

According to MacLennan *et al.* (1955), there is no mechanism of labour in a brow presentation, and therefore no position of the head to consider. Brews (1957) and Moir (1956), however, described anterior and posterior positions and mentioned that delivery as posterior brow is impossible unless rotation to the anterior position occurs. Greenhill (1955) says that, although six brow positions are theoretically possible, left fronto-anterior and right fronto-posterior positions are more commonly seen. Excepting Hellman *et al.* (1950), who found a preponderance of transverse and posterior positions, most authors agree that anterior brow is commoner and carries with it a better prognosis than posterior brow (Brews, 1957; Kenwick, 1953; Moir, 1956; Posner *et al.*, 1957). As shown in Table III, out of 116 cases where records were available the position was anterior in 45.7%, posterior in 25%, transverse in 26.7%, and direct anterior in 2.6%.

TABLE III.—*Positions (No. of Cases)*

| Authors | Fronto-anterior | Fronto-transverse | Fronto-posterior | Direct Anterior |
|---|---|---|---|---|
| Hellman *et al.* (1950) | 8 | 21 | 11 | Nil |
| Kenwick (1953) | 15 | Nil | 6 | " |
| Posner *et al.* (1957) | 12 | 2 | Nil | 3 |
| Skalley and Kramer (1960) .. | 13 | 6 | 3 | Nil |
| Present series .. | 5 | 2 | 9 | " |
| Combined series .. | 53 (45·7%) | 31 (26·7%) | 29 (25%) | 3 (2·6%) |

## Complications

There were five cases of pre-eclamptic toxaemia; the cord was found prolapsed in one case; in four cases labour was prolonged beyond 24 hours, and puerperal sepsis occurred in three cases. One case was admitted after craniotomy had been done outside with no result, the forceps extraction having failed prior to perforation of the head. The perforated head was extracted in the hospital. There was a complete perineal tear and the retained placenta was removed manually. Apart from two cases admitted with obstructed labour and two with ruptured uterus, in one case of maternal death after craniotomy the post-mortem examination revealed uterine rupture. Morris (1953) reported rupture of the uterus in one case, due to attempted internal podalic version, while Hellman *et al.* (1950) found two cases of rupture in their series of 45.

## Mode of Delivery

Spontaneous delivery without any intervention occurred in 6 out of 35 cases (17.1%), including one case where a dead baby weighing 5 lb. 13 oz. (2,636 g.) was delivered naturally as a brow presentation (Table IV). Of the remaining five cases, spontaneous conversion to vertex and face presentation occurred in two and three respectively. In another case, although the head was delivered spontaneously as anterior brow, evisceration was done for obstruction due to foetal ascites.

TABLE IV.—*Mode of Delivery (In Percentage)*

| Authors | Spontaneous Delivery and Low Forceps | Manual Conversion | I.P.V. and Breech Extraction | Craniotomy | Caesarean Section |
|---|---|---|---|---|---|
| Hellman *et al.* (1950)‡ .. | 31·1 | 17·8* | 17·8* | 6·8* | 33·3 |
| Madden (1956)† .. | 35·8 | 15·5 | 46 | | Nil |
| Magid and Gillespie (1957) .. | 50 | 6·25 | 6·25 | | 37·5 |
| Moore and Dennen (1955) .. | 11† | 41 | 25 | | 22 |
| Morris (1953) | 13·2† | 34* | 11·3* | 3·4* | 35·8 |
| Posner *et al.* (1957) | 74 | 4·35* | 8·7* | | 13* |
| Simpson (1950) | 21* | 60·5* | 13·2* | | Nil |
| Skalley and Kramer (1960) .. | 29·6 (18·5†) | 22·2 | Nil | | 48·2 |
| Tancer and Rosanelli (1957) .. | 9·1† | 36·4* | 13·6* | | 41* |
| Present series | 17·1† | 25·7 | 5·6 | 2·8 | 37·1 |

* Percentages calculated from figures given in the article.
† Spontaneous delivery only.
‡ Mature infant only.

Brow position was converted manually to vertex in seven cases and to face in two. Out of these nine cases (25.7%) of conversion, spontaneous delivery occurred in two—one as vertex and the other as face. Forceps extraction was done in six cases of vertex and one case of face presentation, with one neonatal death in a multipara in the former group.

Lower-segment caesarean section was performed in 13 cases (37.1%), including a case of failed forceps. There was only one stillbirth—in a case of obstructed labour admitted with inaudible foetal heart sounds.

Internal podalic version and breech extraction was performed in two cases and one infant died during delivery. Craniotomy was done in one case only. As already mentioned, extraction of the perforated head was carried out in one case. In two cases admitted with ruptured uterus subtotal hysterectomy was performed with good result.

### Mortality

Two maternal deaths occurred in this series (5.7%). One multipara died after craniotomy, the post-mortem examination revealing rupture of the lower uterine segment. In the other case sudden death occurred in a primigravida on the third day of unaided vaginal delivery as a brow presentation. No necropsy was done in this case.

There were eight stillbirths and one neonatal death, the uncorrected perinatal mortality being 25.7% (Table I). If, however, five cases admitted with a dead foetus and one case of congenital foetal anomaly are excluded the corrected perinatal mortality becomes 8.5%.

### Discussion

Antenatal diagnosis of brow presentation is rare and is possible only by radiograph, which is usually taken for some other reason. When diagnosed, correction by posture and pad (Titus, 1950) and by Thorn's manœuvre has been suggested even in early labour (Moir, 1956). But I have had no experience of these measures, and in none of the papers studied is there any mention of personal experience of them. It appears, however, that they are unlikely to be successful in primary brow presentation. In these cases exclusion of contracted pelvis is essential, especially in primigravidae, and in multigravidae with a bad obstetric history. They should be admitted at least two weeks before term and elective caesarean section should be done even in suspected cases of contracted pelvis. In others, waiting for spontaneous onset of labour pains, under close observation, seems justified.

Delivery as brow presentation is seldom possible according to MacLennan *et al.* (1955), and there is no difference of opinion on this point. Moir (1956) states that posterior brow delivery is impossible, whereas in anterior brow it is rarely possible when the baby is small, where the pelvis is big, or where there is a congenital deformity of the infant. In this series one baby weighing 5 lb. 13 oz. (2,636 g.) was delivered spontaneously as anterior brow in a primigravida. Morris (1953) noted two such cases, the birth weight of the babies being 5 lb. 8 oz. (2,495 g.) and 7 lb. 10 oz. (3,458 g.). No other author specified delivery as brow amongst cases delivered spontaneously.

Vaginal delivery after spontaneous conversion is, however, not so rare. Table IV shows the reported incidence, varying from 9.1% (Tancer and Rosanelli, 1957) to 74% (Posner *et al.*, 1957). Eastman (1956) quotes Fink's figure of 43%, while Greenhill (1955) mentions that in 30 to 40% of cases spontaneous conversion to vertex or face is possible. Posner *et al.* (1957) noted that three infants who weighed more than 9 lb. (4,082 g.) were all delivered naturally. In the present series five infants, including two prematures, were delivered unaided—four within 19 hours of onset of labour pains and one within 28 hours. Although Arthure (1957) reported a case where the brow presentation underwent conversion within the pelvis—a similar occurrence was noted in one case of this series—in almost all cases it occurs at or above the pelvic brim. Therefore, even if spontaneous correction does not occur in the majority of cases, it appears worth while to adopt an attitude of watchful expectancy for the first 24 hours of labour in a case where the pelvis is normal and the head is not engaged.

There is an increasing tendency to ignore the place of manual conversion in the treatment of brow presentation mainly because it is a difficult manœuvre and is often unsuccessful. Posner *et al.* (1957) decided against manual conversion because its occasional success is outweighed by the high rate of unaided vaginal delivery and by the complications that may arise in the attempt, although they do not mention what these complications might be. Morris (1953) prefers caesarean section, especially in primigravidae, because of the high rate of failure in conversion. Arthure (1957) considers manual conversion above the brim inadvisable because it is often unsuccessful and is associated with a high rate of foetal mortality.

The conclusions drawn from the present analysis, however, do not support the above views. Conversion was successful in all the nine cases where it was attempted. There was no stillbirth, although one mature infant died after a mid-forceps delivery. According to the results of this series, therefore, manual conversion seems to be a safe manœuvre in cases where spontaneous correction does not occur within 24 hours of labour and where the pelvis is normal and the head is not engaged.

All authors, with the exception of Madden (1956) and Posner *et al.* (1957), have reported a high rate of caesarean section in brow presentation, but only Skalley and Kramer (1960) have given definite indications for the operation. In the present series, out of 13 cases of caesarean section, brow presentation itself was the indication in two only. In the remainder there were other reasons, such as contracted pelvis, foetal distress, and obstructed labour. Only one stillbirth occurred in a case admitted with obstructed labour and a dead foetus. In spite of this satisfactory result from a foetal point of view, the treatment of brow presentation by caesarean section is not justified in all cases. Waiting for spontaneous conversion and manual conversion with or without forceps delivery in selected cases is likely to give a satisfactory overall foetal salvage rate without further increasing the caesarean section rate. If, however, spontaneous correction does not occur within 24 hours of onset of labour pains and manual conversion fails, caesarean section should not be withheld. Caesarean section is also indicated in a case where the brow is engaged, because the chances of natural delivery are remote and manual conversion in the pelvis is unlikely to be successful.

In this series craniotomy has not given satisfactory results. One multigravida died owing to rupture of the lower uterine segment after craniotomy. This indicates that, while the value of craniotomy in selected cases of brow presentation cannot be contested, caesarean section is often a safer procedure even when the foetus is dead. Internal podalic version and breech extraction should have no place in the management of brow presentation. This is so not only because of the associated high rate of foetal wastage and risk of uterine rupture but also because in cases where internal podalic version seems possible manual conversion would be a safer and easier procedure.

### Summary

Thirty-five consecutive cases of brow presentation that occurred in Chittaranjan Seva Sadan College between April, 1953, and January, 1961, have been analysed. The incidence was 1:1,718.

Excluding multiparity, no cause was found in 40% of cases. Primiparity, contracted pelvis, and big infants were thought to be significant causes.

Spontaneous vaginal delivery without any intervention occurred in six cases (17.1%), with one stillbirth. Brow presentation was converted manually in nine cases (25.7%), and one early neonatal death occurred after a mid-forceps delivery. Lower-segment caesarean section was performed in 13 cases (37.1%). There was no foetal loss in 12 cases admitted with audible foetal heart sounds.

Maternal mortality and corrected perinatal mortality were 5.7% and 8.5% respectively.

Management of brow presentation has been discussed.

I am indebted to Dr. Subodh Mitra, the Director, for permission to publish the hospital records and for his guidance. I also thank Dr. P. K. Biswas for his helpful advice and criticism in the preparation of this paper.

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# ABO GROUPS AND RH GENOTYPES IN THE ELDERLY

BY

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The following series is reported in the hope that it will contribute something to the present picture about blood groups and disease associations, and perhaps help towards planning further work.

The study was started after a survey of ABO groups and Rh genotypes in paternal grandparents in cases of haemolytic disease of the newborn, a specially selected group of people in whom certain deviations in the proportions of ABO groups and Rh genotypes were expected. The differences which occurred, however, could not all be explained on this score, and it seemed desirable to investigate whether age selection was having an effect. Hence this study of other elderly persons was undertaken; but as certain disease associations with ABO groups had been reported it was decided to compare a group of in-patients in geriatric units with a healthy elderly group.

## Material

In all, 633 persons over 64 years of age were tested. Investigations of 497 samples were made between April and July, 1958, and all patients available in the wards at the time of testing were used to form a "geriatric group" representative of the usual diseases of the elderly. The "healthy group" were mainly active members of "Over 60s" clubs, but a few were healthy donors who had been "retired" because they had reached the age of 65 years. An additional 136 persons were tested in July, 1959, to confirm the findings or otherwise, and as the same difference in blood-group proportions was apparent the results have been pooled.

The sex, age ranges, and mean ages were as follows:

| | | | | |
|---|---|---|---|---|
| Geriatric patients | 184 males | 65–93 years. | Mean age 75·1 years | |
| | 168 females | 65–104 ,, | ,, ,, 76·4 | ,, |
| Healthy elderly persons | 125 males | 65–89 ,, | ,, ,, 71·6 | ,, |
| | 156 females | 65–82 ,, | ,, ,, 70·7 | ,, |

The geriatric cases were placed rather arbitrarily into broad categories according to the recorded diagnoses, the miscellaneous group comprising all conditions with fewer than three cases. Table I shows the wide range of illnesses, and the similarity in this respect between the male and female patients.

TABLE I.—*Recorded Diagnoses and ABO Groups of 352 "Geriatric Cases"*

| | Male | Female | O | A | B | AB |
|---|---|---|---|---|---|---|
| Carcinoma | 21 | 16 | 22 | 12 | 3 | — |
| Congestive cardiac failure | 16 | 16 | 17 | 11 | 3 | 1 |
| Anaemia and blood diseases | 7 | 12 | 11 | 6 | 2 | — |
| Fractures | 4 | 11 | 10 | 4 | 1 | — |
| Coronary thrombosis | 14 | 9 | 12 | 9 | 2 | — |
| Cerebral thrombosis and hemiplegias | 19 | 19 | 17 | 14 | 4 | 3 |
| Bronchitis, pneumonia, etc. | 16 | 8 | 9 | 11 | 2 | 2 |
| Arteriosclerosis | 4 | 12 | 10 | 3 | 2 | 1 |
| Pernicious anaemia | — | 6 | 4 | 2 | — | — |
| Gall-bladder conditions | 3 | 6 | 5 | 3 | 1 | — |
| Arthritis | 4 | 3 | 1 | 5 | 1 | — |
| Diabetes | 6 | 5 | 5 | 5 | 1 | — |
| Haematemesis | 7 | 4 | 5 | 4 | 2 | — |
| Genito-urinary conditions | 27 | 4 | 14 | 10 | 6 | 1 |
| Miscellaneous (including disseminated sclerosis, senility, etc.) | 32 | 36 | 37 | 22 | 6 | 3 |
| Not recorded | 4 | 1 | 1 | 4 | — | — |
| Totals | 184 | 168 | 180 | 125 | 36 | 11 |

The Rh genotype tests were performed using the four more common anti-Rh sera, and anti-e where necessary. Certain "expected errors" occur within different Rh genotype groups owing to the absence of anti-d serum, and these are dealt with later. As regards technical errors, identical Rh testing-sera, carefully checked for specificity, were used in the two groups of cases.

## Results

### ABO Groups

Among the group A and AB individuals the proportion belonging to the subgroup $A_2$, 22% in the geriatric group and 19% in the healthy group, was as expected. Table II shows the ABO distribution. There are no real differences between females in the geriatric and healthy groups. Among the males, however, there is a decrease in group O and an increase in group A in the healthy group compared with the geriatric group which is significant ($\chi^2_{(1)} = 5.165$. $P < 0.025$).

TABLE II.—*ABO Groups of 633 Persons Over 64 Years of Age*

| Group | Geriatric Group | | | | | | Healthy Group | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Total | | Male | | Female | | Total | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| O | 94 | 51·1 | 86 | 51·2 | 180 | 51·1 | 46 | 36·8 | 75 | 48·1 | 121 | 43·1 |
| A | 64 | 34·8 | 61 | 36·3 | 125 | 35·5 | 58 | 46·4 | 61 | 39·1 | 119 | 42·3 |
| B | 22 | 11·9 | 14 | 8·3 | 36 | 10·2 | 14 | 11·2 | 15 | 9·6 | 29 | 10·3 |
| AB | 4 | 2·2 | 7 | 4·2 | 11 | 3·1 | 7 | 5·6 | 5 | 3·2 | 12 | 4·3 |

It is noted that the A/O ratio in the healthy elderly men, 46/37, is reversed compared with the healthy elderly females, 39/48, and with both the males and females in the geriatric group, 35/51, 36/51.

A certain validity is given to these ABO differences by comparing (Table III) the overall ABO proportions in the elderly persons with the group frequencies found in 1,482 new donors in Newcastle City tested over approximately the same period, and with the percentage figures from a large-scale survey of donors in this region by Fraser Roberts (1953). Agreement is close, and there is obviously no significant difference between the donor figures reported by Fraser Roberts and the overall ABO proportions among the elderly persons. However, when the same donor figures are compared (O *v.* A) with the healthy elderly males, the latter group again shows a significant increase in group A ($\chi^2_{(1)}=6.005$. P <0.025).

TABLE III.—*ABO Groups Percentage in Donors and Elderly People*

| | Group | | | | No. Tested |
|---|---|---|---|---|---|
| | O | A | B | AB | |
| Elderly persons .. .. | 47·6 | 38·5 | 10·3 | 3·6 | 633 |
| New donors. Newcastle City | 50·4 | 36·7 | 9·7 | 3·2 | 1,482 |
| Donors (Fraser Roberts, 1953) .. .. .. | 49·5 | 38·6 | 9·1 | 2·8 | 54,579 |

**Rh Genotypes**

The Rh (D) negative proportion—that is, including samples belonging to subgroup Cde/cde or cdE/cde—was 14.8% in the geriatric group and 18.5% in the healthy group. The remaining Rh (D)-positive samples are shown as D/D homozygous or D/d heterozygous in Table IV and, for comparison, random proportions are shown taken from Race and Sanger (1954. Pooled results).

There is very close agreement between the overall proportions of homozygotes and heterozygotes among all the elderly persons and the random proportions. There is, however, a highly significant difference between the healthy and geriatric groups showing as a deficiency of heterozygotes D/d and an increased proportion of homozygotes D/D among the healthy elderly persons ($\chi^2_{(1)}=9.259$. P <0.005). Again this is most apparent among the healthy elderly males ($\chi^2_{(1)}=6.621$. P <0.025), although the difference between males and females in this respect is not significant (interaction in Table IV), the latter showing the same trend.

TABLE IV.—*Proportion of D/D and D/d Among 528 Persons Over 64 Years of Age*

| | | Homozygote | | Heterozygote | | Total |
|---|---|---|---|---|---|---|
| | | No. | % | No. | % | |
| Geriatric | Male .. | 56 | 36·4 | 98 | 63·6 | 154 |
| | Female .. | 51 | 35·2 | 94 | 64·8 | 145 |
| | Total | 107 | 35·8 | 192 | 64·2 | 299* |
| Healthy | Male .. | 55 | 53·4 | 48 | 46·6 | 103 |
| | Female .. | 58 | 46·0 | 68 | 54·0 | 126 |
| | Total | 113 | 49·3 | 116 | 50·7 | 229 |
| All elderly persons: Grand total .. | | 220 | 41·7 | 308 | 58·3 | 528 |
| Random .. | | 626 | 42·1 | 861 | 57·9 | 1,487 |

$\chi^2_{(1)}$ Male *v.* female .. .. 0·30, not significant
$\chi^2_{(1)}$ Healthy *v.* geriatric .. .. 9·78, P<0·005.
$\chi^2_{(1)}$ Interaction (by difference) .. 2·03, not significant
$\chi^2_{(3)}$ 12·11

* One $R_3r^?$ excluded, not tested with anti-e.

Once more there is a reversal of a ratio among the healthy elderly men: D/D homozygote to D/d heterozygote, 53:47, compared with healthy elderly women, 46:54, and with male and female geriatric cases, 36:64 and 35:65 respectively.

As seen in Table V the increase in D/D homozygotes in the healthy male group was mainly caused by an increase in the number in the subgroup $R_1R_2$, the proportion of which was 26.2%. The random proportions taken from Race and Sanger (1954) are also shown.

When anti-e serum is used, as in this series, the largest error involved when the most probable genotype in any reaction group is guessed is reduced from approximately 20% to 6%. This means that in a random sample approximately 12% of those thought to be heterozygous D/d might be homozygous D/D, and in approximately 14% the guess is wrong in the reverse direction. Thus, having regard only to the number in the two groups of cases, one or two in the geriatric group shown as homozygous might be heterozygous, but this would not alter the findings. However, there are more homozygotes in the healthy group and more heterozygotes in the geriatric group. Thus, although there is no way of showing either whether the "errors" occur as in unselected persons, or whether the "errors" are the

TABLE V.—*Rh Genotype Results of 633 Persons Over 64 Years of Age*

| | | | $R_2R_2$ | $R_1R_2$ | $R_1R_1$ | $R_2r$ | $R_2r'$ | $R_1r'$ | Others | d/d | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Geriatric cases | Male | No. | 1 | 25 | 30 | 2 | 27 | 69 | 1* | 29† | 184 |
| | | % | 0·6 | 16·1 | 19·4 | 1·3 | 17·4 | 44·5 | 0·6 | (15·8) | |
| | Female | No. | 3 | 25 | 23 | 1 | 19 | 74 | — | 23‡ | 168 |
| | | % | 2·1 | 17·2 | 15·9 | 0·7 | 13·1 | 51·0 | | (13·7) | |
| | Total | No. | 4 | 50 | 53 | 3 | 46 | 143 | 1 | 52 | 352 |
| | | % | 1·3 | 16·7 | 17·7 | 1·0 | 15·3 | 47·7 | 0·3 | (14·8) | |
| Healthy group | Male | No. | 1 | 27 | 26 | 2 | 10 | 36 | 1 $R_1R_2$ | 22§ | 125 |
| | | % | 1·0 | 26·2 | 25·2 | 1·9 | 9·7 | 35·0 | 1·0 | (17·6) | |
| | Female | No. | 3 | 26 | 29 | 3 | 11 | 54 | — | 30‖ | 156 |
| | | % | 2·4 | 20·6 | 23·0 | 2·4 | 8·7 | 42·9 | | (19·2) | |
| | Total | No. | 4 | 53 | 55 | 5 | 21 | 90 | 1 | 52 | 281 |
| | | % | 1·7 | 23·1 | 24·0 | 2·2 | 9·2 | 39·3 | 0·4 | (18·5) | |
| Random | | No. | 38 | 257 | 327 | 39 | 216 | 606 | 4 $R_1R_2$ | 311¶ | 1,798 |
| | | % | 2·6 | 17·3 | 22·0 | 2·6 | 14·5 | 40·8 | 0·3 | (17·3) | |

Percentages are of Rh (D) positive, except those in parentheses, which are overall Rh (D)-negative proportions.
* Not tested with anti-e $R_2r^?$. † Includes 1 R′r and 1 R″r. ‡ Includes 1 R″r. § Includes 1 R′r. ‖ Includes 1 R′R″. ¶ Includes 17 R′r and 13 R″r.

same in the two groups, it could be that one homozygote in the healthy group, but up to four heterozygotes in the geriatric group, are wrong guesses. This would somewhat reduce the significance of the findings.

### Discussion

A slight but significant sex difference in ABO blood-group frequencies was recognized in 1943 when Fisher and Fraser Roberts, in a very large series, found the proportion of group A in men to be higher than in women, and that more of the latter were group O. This is very apparent in the healthy group in this series of elderly people but not in the geriatric group.

Age stratification of ABO blood group frequencies has also been looked for extensively (Fraser Roberts, 1948) and not found, but the author stated that the evidence covered adequately only donor ages approximately 18–60 years.

Aird *et al.* (1953) reported that carcinoma of the stomach is more common among group A individuals, and the evidence has been stated to be overwhelming (Fraser Roberts, 1959). Manuila (1958), however, thinks that the evidence for or against this association is not conclusive. The difference in group A proportions reported by Aird *et al.* between the gastric carcinoma cases and the hospital controls for Newcastle was less than the difference between the geriatric and healthy group in this series. Unfortunately their cases were not subdivided for age, although in a later report (Aird *et al.*, 1954) group frequencies by sex were given for some of the patients with carcinoma of the stomach drawn from a number of hospitals (locality unspecified). The authors noted that their figures did not exclude the possibility that the whole of the excess of group A in cancer of the stomach occurs in men, but thought this unlikely. In this report also it was noted that the gastric ulcer cases, which were drawn from three regions —London, Manchester, and Newcastle—showed that in both sexes the patients of group A were older than the patients of group O.

It is of interest also that in a series of 119 cases of gastric carcinoma (Jennings *et al.*, 1956) an association between group A and carcinoma of the pyloric end of the stomach was found, but only in men. And, again, in a study of blood groups in diabetes mellitus McConnell *et al.* (1956) found an excess of group A in diabetic men but not women.

In the present series the division is a simple one. One group was made up of in-patients in hospital, at least temporarily bedridden ; the other of elderly people healthy enough to be active and ambulant. The significant change in the ABO groups—an increased proportion of group A—is localized to the healthy elderly male group. The series is reported in the hope that further work may elucidate whether it is mainly a northern phenomenon, and perhaps associated with the higher incidence of carcinoma of the stomach in the north, or whether some other selection is resulting in group A being more frequent among elderly people, and giving the appearance of carcinoma of the stomach, a disease of the elderly, being more frequent in group A persons.

So far as the Rh genotype differences are concerned, the heterozygote D/d, as in haemolytic disease of the newborn, again appears to be at a disadvantage, although among the homozygotes D/D in the healthy group it is the proportion of the " mixed " $R_1R_2$ which was most raised.


### Summary

The ABO groups and Rh genotypes are reported on 633 persons over 64 years of age. These are divided into in-patients in geriatric units covering a wide range of illnesses, and a healthy elderly group. Significant differences in ABO distribution, showing as an increased proportion of group A, occurred in the healthy elderly male group. A significant increase in the proportion of homozygotes D/D among the healthy group is reported, most apparent among the males.

It is hoped that this series will help towards planning future work.


My thanks go to Dr. G. J. Murray, Dr. T. H. Bates, and Dr. E. Woodward Williams, consultant physicians, for making available the patients in their geriatric units. Also to Dr. Angus Dodds, recently at Hexham General Hospital, for his care in collecting samples from one unit, and to Dr. Judith Hay and Dr. T. D. Davies for collecting so many others. Grateful acknowledgments are also due to Dr. George Knox, Department of Child Health, University of Durham, for the statistical findings reported and for his advice.

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# Preliminary Communications

## A New Chromosome Abnormality in Chronic Granulocytic Leukaemia

The presence of an abnormally small acrocentric chromosome ($Ph^1$ chromosome) has been described as a constant feature in the leucocytes of a high proportion of patients with chronic granulocytic leukaemia (Nowell and Hungerford, 1960a, 1960b ; Baikie *et al.*, 1960 ; Tough *et al.*, 1961). We have confirmed this finding in four consecutive cases of chronic granulocytic leukaemia. In addition we now report a new abnormality occurring in one of these four patients. The leucocytes of this individual show a replacement of two of the smallest acrocentrics by abnormal chromosomes, one of which corresponds to the $Ph^1$, whereas the other is a minute fragment. The two abnormal structures are present either singly or in combination in the majority of the cells which have been analysed.

#### CASE REPORT

The patient, a man aged 34, was first diagnosed in August, 1954, as suffering from chronic granulocytic leukaemia. He was treated with splenic *x*-irradiation, $^{32}P$, and busulphan, the disease remaining in good remission until March, 1961, when it entered an acute phase. After the administration of 6-mercaptopurine and prednisone a further remission occurred. Whereas in March, 1961, the marrow contained a high proportion of blast cells, which were also present in the blood, both marrow and blood showed a practically normal composition in June, and this remission has continued to date.

*Methods of Examination.*—The marrow was examined three times. The first examination, in March, 1961, was at the height of the acute exacerbation, when sternal marrow was obtained one hour after the intravenous administration of 6 mg. of demecoline ("colcemid") as suggested by Bottura and Ferrari (1960). The other two examinations were made in June and July, 1961, without previous administration of demecoline. The marrow samples were in each instance placed direct into hypotonic sodium citrate and treated according to the method of Kinlough *et al.* (1961), except that the final films were not made by squashing but by air-drying.

Three cultures of the patient's blood were made by the method of Moorhead *et al.* (1960) during July and August, 1961. During this period the blood count was normal except for the presence of a few (2–5%) myelocytes.

## Results

*Marrow.*—The three specimens were examined for chromosome number and abnormalities; the findings are shown in Table I. In all specimens the diploid mode was 46 chromosomes. The Ph¹ chromosome was easily identified, and its prevalence is indicated in Table I. There was a second, much smaller, chromosome, which replaced a second small acrocentric and is shown as "minute" in

TABLE I.—*Results of Marrow Examinations*

| Date | Chromosome Number (Diploid Cells) | | | | | Chromosome Abnormality | | | | Total Cells Counted |
|---|---|---|---|---|---|---|---|---|---|---|
| | <44 | 44 | 45 | 46 | >46 | Ph¹ | "Minute" | Ph¹+ "Minute" | Normal | |
| March | 3 | 2 | 7 | 38 | 0 | 16 | 9 | 15 | 10 | 50 |
| June | 3 | 2 | 5 | 40 | 0 | 8 | 9 | 9 | 24 | 50 |
| July .. | 1 | 3 | 4 | 29 | 0 | 4 | 8 | 5 | 20 | 37 |

Table I and pictured in Fig. 1. It can be seen that some cells contained the Ph¹, others the "minute," and others still both the abnormal chromosomes. A translocation between chromosome No. 2 and one of the 6–12 group was seen in some cells (Fig. 2). This was present in 9 of 25 and 7 of 15 cells which could be fully analysed in the March and June specimens respectively. All cells containing the translocation also contained the Ph¹, and some contained the "minute." Furthermore, the marrow samples showed increasing numbers of tetraploid or near tetraploid metaphase plates. There were 14, 23, and 33 tetraploids among 100 cells examined respectively in each of the March, June, and July specimens. The modal number was 92 in those plates in which precise counts could be made (Fig. 3).

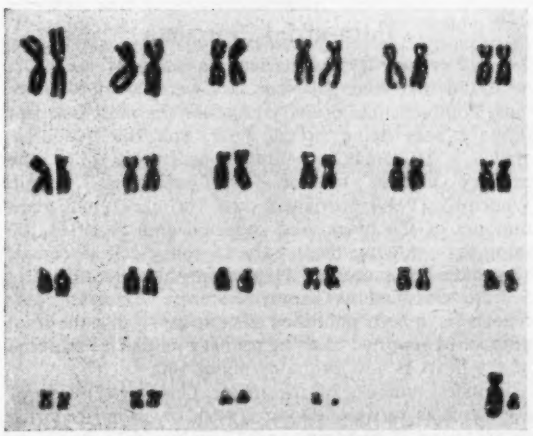

FIG. 1.—Karyogram of cell from direct marrow preparation: 46 chromosomes. In the place of the last pair of autosomes there are one abnormal small acrocentric chromosome (Ph¹) and one smaller fragment (the "minute").

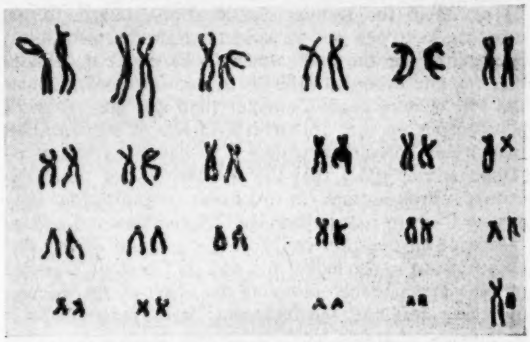

FIG. 2.—Karyogram of cell from direct marrow preparation: 46 chromosomes. One member of the second pair of chromosomes shows an abnormally long lower arm. This appears to have arisen from a translocation in which one of the 6–12 group of chromosomes (Denver classification) was also involved. This abnormally short chromosome has been placed to the right of the second row of chromosomes. The X and Y chromosomes are shown to the right of the bottom row. The Ph¹ chromosome is also present in the "22" position.

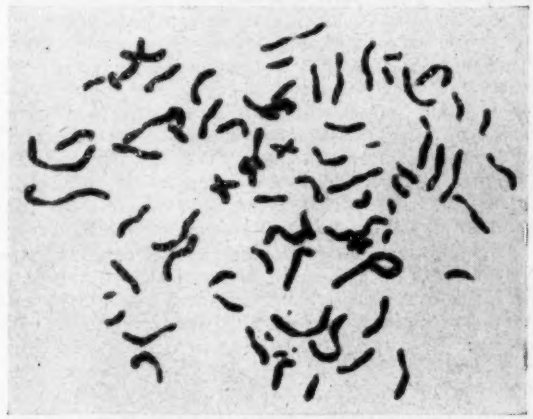

FIG. 3.—Polyploid (tetraploid) cell from direct marrow preparation showing two "minutes."

*Blood.*—The chromosome numbers are shown in Table II. Again the diploid mode was 46. Only three "minutes" were identified, and the Ph¹ chromosome was seen only once. Five of 150 cells examined were tetraploid or near tetraploid. A possible translocation was seen in three cells in the August culture but in neither of the other two. Chromosome breaks were seen in four figures.

TABLE II.—*Results of Blood Cultures*

| Date of Culture | Chromosome Number (Diploid Cells) | | | | | Chromosome Abnormality | | | | Total Cells Counted |
|---|---|---|---|---|---|---|---|---|---|---|
| | <44 | 44 | 45 | 46 | >46 | Ph¹ | "Minute" | Ph¹+ "Minute" | Normal | |
| 14/7/61 | 0 | 1 | 1 | 9 | 0 | 0 | 0 | 0 | 11 | 11 |
| 21/7/61 | 0 | 0 | 1 | 11 | 2 | 0 | 0 | 0 | 14 | 14 |
| 17/8/61 | 3 | 1 | 3 | 36* | 6 | 1 | 3 | 0 | 49 | 53 |

* Also 4 polyploid cells.

## DISCUSSION

The work of the Philadelphia and Edinburgh groups has made it clear that the Ph¹ chromosome is the only constant chromosome abnormality found in the leukaemias. Nowell and Hungerford (1960a, 1960b) found it in seven and Tough *et al.* (1961) in 13 out of 18 patients with chronic granulocytic leukaemia. The abnormality is the result of loss of chromatin material from one of the smallest acrocentric chromosomes (No.

21 or 22 in the Denver classification), but no direct evidence has been put forward to show the mechanism responsible for the loss. It could be either a deletion or a translocation, with the distinction uncertain because the Ph¹ is only slightly smaller than the normal small acrocentrics, so that collateral evidence of translocation would be difficult to collect. It has been suggested (Ohno *et al.*, 1961) that the involvement of the acrocentric chromosomes in nucleolar organization may expose them to risk of damage. A fundamental and so far unsolved question concerns the relation of the Ph¹ chromosome to the leukaemic process; does its presence precede and possibly stimulate the onset of the disease, or is it a result of the leukaemic transformation? It is unlikely to result from treatment, since it has been found in untreated patients.

In our material there were two abnormal small acrocentric chromosomes, the Ph¹ and the "minute." These were present in a high proportion of cells in all three marrow specimens, during both the acute exacerbation and the subsequent remission of the disease. There were also a good many apparently normal mitoses, which was to be expected in a tissue with a mixed cell population like the marrow. Both abnormalities appeared to characterize fundamentally altered—that is, leukaemic—cells; and, since the composition of the marrow specimens was very different in the first specimen compared with the second and third specimens, it appears that the Ph¹ and the "minute" acrocentrics were contained in leukaemic blasts as well as myelocytes which could not otherwise be distinguished from their normal counterparts.

The new abnormality was interesting because of the extremely small size of the chromosome. If this had arisen from a translocation, one would have expected to find a reciprocal abnormality in another chromosome. In over 50 completely analysed figures we have not seen any suggestion of this. At the same time, the "minute" was itself capable of further division; many of the tetraploid figures contained two "minutes" (Fig. 3). We suggest that this chromosome abnormality arose from a deletion of chromatin material either before or after the onset of leukaemia. The same may well be true of the Ph¹ chromosome, and both might be the consequence of damage during nucleolar organization, as suggested by Ohno *et al.* (1961).

The rather constant translocation between the No. 2 and one of the 6–12 chromosomes was probably the result of treatment, either radiotherapy or chemotherapy. It occurred only in cells carrying the Ph¹, and its high frequency suggests that it must have conferred some selective advantage on the cells carrying it. The increasing proportion of tetraploid mitoses was of interest in view of the fact that polyploidy has been found associated with radio-resistance in some other pathological materials (De, 1961).

The three blood cultures showed, in strong contrast to the direct (non-cultured) marrow preparations, a notable paucity of all types of chromosomal abnormality. This suggests that the dividing cells in the blood were mostly non-leukaemic. The blood picture was practically normal on all occasions, and it is probable that most of the mitoses arose from large lymphocytes or monocytes which, in normal blood, are the only cells capable of division (Bond *et al.*, 1958). In the type of case here described the direct marrow preparations had thus a notable advantage over those derived from blood cultures, in that they yielded a far higher proportion of the characteristic abnormal mitoses. This finding is in line with the arguments put forward by Sandberg *et al.* (1960, 1961). It also disposes of the contention that the Ph¹ chromosome may be an artifact produced in culture (Trujillo *et al.*, 1961).


### SUMMARY

Repeated examination of the bone-marrow of a patient with chronic granulocytic leukaemia showed the presence of the Ph¹ chromosome as well as that of a hitherto undescribed minute chromosome replacing a second small acrocentric and probably originating from a deletion of chromatin material. These abnormalities were more easily found in direct marrow preparations than in cultures of the peripheral blood. They were present during remission as well as during an acute exacerbation of the disease.



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# Medical Memoranda

## Intra-atrial Sarcoma

When Prichard (1951) reviewed tumours of the heart he found that secondary tumours were 20 to 40 times more common than primary tumours, the most frequent primary sites being breast, lung, and the lymphatic system. Myxomas constituted nearly 50% of the primary cardiac tumours, with sarcomas second. Whorton (1949) reviewed the primary malignant tumours of the heart, and collected and classified 100 sarcomas. Among these were 18 round-cell sarcomas, 18 spindle-cell sarcomas, 11 pleomorphic sarcomas, and 5 were classified as leiomyosarcomas. Isolated case reports have been published since then, so that the total number of reported cases of primary malignant tumours of the heart is now probably about 160.

Primary tumours of the major blood-vessels are of even greater rarity—Giaccai (1949), reviewing reported cases, found 26 (9 benign and 17 malignant). Some are similar to the present case.


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Baldwin (1910) described a pedunculated sarcoma arising from the region of the mouth of the pulmonary veins and almost filling the left auricle. Ausbüttel (1939) described a pleomorphic-celled sarcoma arising in the right pulmonary vein, proliferating as far as the left atrium. Ravid and Sachs (1943) reported a primary myxosarcoma of the left auricle and pulmonary vein, and Cumming and Shillitoe (1957) described a tumour with the features of an osteogenic sarcoma, which arose from the right superior pulmonary vein, and grew into the left atrium, obstructing the mitral opening by a ball-valve mechanism.

The following case report describes a somewhat similar tumour in a woman of 35.

## CLINICAL HISTORY

A 35-year-old housewife was first seen at the Royal Victoria Hospital, Belfast, on November 30, 1959. She gave a two-months history of exertional dyspnoea and of three episodes of haemoptysis. On clinical examination there were no abnormal physical signs. A chest *x*-ray film showed a prominent pulmonary conus but no evidence of a lung lesion, the Mantoux 1:10,000 was positive, and the E.S.R. was 65 mm. in the first hour (Westergren). Over the next four weeks she was examined several times and was admitted on December 26. There had been no change in the history of her complaint and no history of rheumatic fever could be elicited. On examination an early diastolic murmur had appeared at the lower end of the sternum, and a mid-diastolic murmur at the apex after exercise. The blood-pressure was 125/80 mm. Hg and the pulse was in sinus rhythm. The chest *x*-ray film was as before. E.S.R. was repeatedly elevated (85 mm., 38 mm., 39 mm.), but there was no fever and no clinical or laboratory evidence of rheumatic or bacterial endocarditis. E.C.G. was non-contributory.

Some days after her admission there was a marked change in her mental state—formerly one of slight withdrawal and apprehension. She began to shout, talked in a disconnected manner, refused treatment, expressed delusions that she was being poisoned, and demanded to be allowed home. She was seen by a psychiatrist, who advised admission to Purdysburn Mental Hospital, where, on chlorpromazine 50 mg. t.d.s., she settled down quite rapidly. While there her E.S.R. was persistently elevated (40–50 mm. in the first hour), and after further mild haemoptyses she was readmitted to the Royal Victoria Hospital on February 12, 1960. The physical signs were very much as before, with a heaving right ventricular outflow tract, an early diastolic murmur, and an inconstant apical mid-diastolic murmur. Three days after her second admission she became tense and hallucinated, and expressed delusions of persecution. This state was followed by a period in which she was virtually catatonic. *X*-ray screening at this time suggested left atrial enlargement, and the causes of mitral-valve obstruction, either by valve disease or tumour, were being considered when her mental state necessitated her readmission to the mental hospital, where she again settled down.

Three weeks later she was readmitted to the general hospital with massive haemoptysis, requiring blood transfusion, and at this time poor air entry at the left apex was noted. She was transfused, and, while she recovered physically, she became agitated and the demonstration of definite suicidal tendencies expedited her further transfer to the mental hospital, whence she returned on March 26, after another massive haemoptysis. At this time there was a tricuspid systolic murmur and a markedly heaving right ventricular outflow tract, and a tentative diagnosis of pulmonary embolism was made. However, no peripheral source of emboli could be found and all murmurs quickly disappeared. She remained dull and withdrawn and complained of unpleasant "voices" in her head, but it was felt that investigation should proceed.

Cardiac catheterization was carried out on March 31. The catheter passed easily into the right pulmonary artery and the "wedge" pressure was 11 mm. Hg at rest, rising to 17 mm. Hg on exercise. The mean pulmonary artery pressure was 20 mm. Hg. It was felt that this ruled out mitral-valve disease as a cause of the haemoptysis, and causes of intermittent pulmonary hypertension, such as left atrial myxoma, were being considered, when, the following morning, she had a further massive haemoptysis and died.

## NECROPSY FINDINGS

The state of nutrition was poor. No peripheral oedema was present, nor were there effusions in any of the serous cavities.

The heart was not enlarged generally, though the left atrium was held in a dilated position by a firm mass within. On opening the atrium this was seen to be a tumour, measuring 6 by 5 by 5 cm., almost completely filling the atrium, and extending as a rounded plug into the mitral opening (Fig. 1). The mitral-valve cusps were quite

FIG. 1.—Heart viewed from behind. The tumour can be seen arising from the left pulmonary vein (see arrow), spreading into the left atrium, and extending down as far as the mitral-valve ring.

normal. The surface of the tumour was smooth, though slightly lobulated, and on section it was greyish white in colour, of very firm consistency, and showed a few small areas of haemorrhage. Although loosely adherent to the thickened atrial endocardium it could be easily stripped as far as the ostium of the left superior pulmonary vein. Here the tumour was intimately attached to the vein wall and had expanded therein to a diameter of 2.5 cm. Prolongations of tumour extended distally along the tributaries of the vein for 2–3 cm. The left inferior pulmonary vein was partially occluded by tumour, and the lower branch of this vein contained a recent thrombus. At no point had the tumour penetrated the walls of the veins or atrium.

The trachea and bronchi contained large quantities of recent blood and blood clot. Both lungs showed a reddish mottling, visible from the pleural surface and on section, due to recently inhaled blood. The tumour had not invaded neighbouring bronchi or vessels. The lungs also contained some oedema. Otherwise the texture of the right lung appeared quite normal. The upper lobe of the left lung, however, felt firm and was grey in colour, suggesting fibrosis.

No tumour metastases were located in spite of a complete and careful examination. There were no signs of disease in the remaining organs.

### HISTOLOGY

The tumour was a spindle-cell sarcoma. It was composed of interlacing bundles of elongated cells with wide variation in the size and shape of their nuclei, some being very large and of bizarre shape and showing occasional mitotic figures (Fig. 2). The cell cytoplasm was faintly eosinophilic with

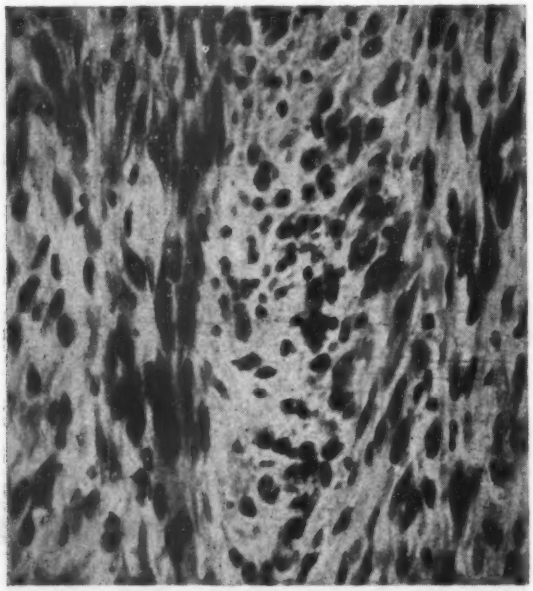

FIG. 2.—Photomicrograph of tumour. (H. and E. ×300.) Note elongated spindle-shaped cells with large hyperchromatic nuclei.

haematoxylin and eosin. Special staining, employing Lendrum's picro-Mallory and Mallory's phosphotungstic acid haematoxylin, revealed the presence of muscle fibres. No cross-striations could be demonstrated with Heidenhain's haematoxylin.

At its point of origin from the left superior pulmonary vein the tumour was intimately associated with the vein wall, so that the two could not be separated. No extension was present outside the wall. The central areas of the tumour showed slight haemorrhage and much necrosis. Organized thrombus had been incorporated on the surface of the tumour.

Sections from the upper lobe of the left lung were of interest in that they showed an extensive interstitial fibrosis. The alveolar walls were greatly thickened by fibroblastic proliferation, with relatively few blood vessels. There was considerable variation in the size of the alveoli, and many were lined by a low cuboidal epithelium. Some contained collections of heart-failure cells, and recently aspirated red cells were also present. The small and medium-sized pulmonary arteries in this area showed a noticeable narrowing of their lumen by medial hypertrophy and intimal proliferation, resembling an obliterative arteritis.

Sections from the left lower lobe and the right lung showed red cells in bronchi, bronchioles, and alveoli. There was some distension of the broncho-pulmonary veins. No arterial changes were present in these areas. Occasional groups of haemosiderin-containing mononuclears were present.

Sections of the other organs, including the brain, revealed no lesion.

### COMMENT

This case report is of a leiomyosarcoma of the left superior pulmonary vein growing into the left atrium, causing retrograde thrombosis of the left pulmonary veins, haemorrhage from the broncho-pulmonary anastomoses, and death by asphyxiation. Among the points of interest are the rarity of the tumour in the published literature, and the changes in the lung similar to those described by Andrews (1957) subsequent to pulmonary vein thrombosis, resembling interstitial fibrosis.

The clinical picture of the findings on investigation suggested left atrial obstruction. It was felt, however, that the normal wedge pressure in the right lung field excluded mitral stenosis and made left atrial myxoma unlikely. Had the wedge pressure, in addition, been recorded in the left upper lobe, the diagnosis of localized obstruction to the pulmonary venous return—probably due to tumour—would have been suggested, and the possibility of pneumonectomy and removal of the tumour might then have been considered. The accelerated E.S.R. was probably of significance, as MacGregor and Cullen (1959) have remarked on it in cases of intra-atrial myxoma; there was, however, no fever.

The mental state delayed and prevented attempts at accurate diagnosis; her symptoms were thought to be those of an acute schizophrenic reaction, with paranoid delusions, agitation, and suicidal tendencies, progressing to withdrawal and retardation. It is not clear what factors, if any, in her clinical illness can be incriminated in the production of the mental disturbance. Her premorbid personality was stable and there was no previous history of mental illness in the patient or her family. It is possible that abnormal tissue metabolism as a result of malignant disease, or the recurrent psychic trauma of impending cardiological investigation and surgery, could have contributed to it.

We thank Drs. T. T. Fulton, J. F. Pantridge, and D. M. Gardner, and Professor J. H. Biggart for their help and advice.

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# Reviews

## INTRODUCTION TO JUNG

*C. G. Jung.* By E. A. Bennet. (Pp. 165+viii; illustrated. 21s.) London: Barrie and Rockliff. 1961.

C. G. Jung is one of the outstanding figures of this century. His researches have played an important part in developments in many different branches of psychiatry, psychology, and associated fields of knowledge during the last 50 years. Yet his contributions are regarded with suspicion, and sometimes contempt, by many psychiatrists. Few of these have studied his works seriously and it is to be hoped that this book, by one of Jung's closest friends and pupils, will be a valuable corrective to such ill-considered judgments.

The author does not set out to give a detailed exposition of Jung's researches but to depict some key aspects of his work in the setting of his personality. Dr. Bennet is a good story-teller, and with lively anecdotes he traces the beginnings and evolution of Jung's main ideas and methods in the dreams and fantasies of his childhood, in early psychiatric and experimental work, and in his friendship, collaboration, and eventual break with Freud. He points out that of those involved in the highly emotional atmosphere of this break Jung alone set out to study the clash as a psychological phenomenon. From his reflections there emerged the celebrated theory of psychological types.

This determination to study as objectively as possible any aspect of life or experience and his respect for the depth and breadth of human endeavour and aspiration led Jung into fields which at first sight seem to be remote from the consulting-room. It is his researches into comparative religion, mythology, alchemy, and astrology which have caused many conventional people to dismiss him as "mystical." Dr. Bennet points out how inappropriate this adjective is either to Jung's personality or to his work. Jung was an undogmatic empiricist who constantly sought for new methods by which to extend psychological research. He never lost contact with his medical background and was always concerned with the relevance of his work to the situation of the doctor with his patient.

The immense volume of his writings, the unfamiliarity and complexity of much of the material, and some obscurity of expression lead to difficulties in reading Jung. Although Dr. Bennet's brief notes on the central ideas are of necessity patchy, his intimate knowledge of his subject and the clarity and directness of his style make this book an excellent introduction to Jung's thought.

R. F. HOBSON.

## VALVULAR LESIONS IN THE OLD

*Valvular Disease of the Heart in Old Age.* By P. D. Bedford, M.D., M.R.C.P., and F. I. Caird, D.M., M.R.C.P. (Pp. 194+x; illustrated. 30s.) London: J. and A. Churchill, Ltd. 1960.

This little monograph has much to commend it. It is neither a system of geriatrics nor a textbook of cardiology, but proves to be a wholesome and welcome account of the authors' experiences in the clinical recognition and course of valvular disease of the heart in an elderly community. Their review is based on 419 patients, carefully studied over a period of six and a half years at the Geriatric Unit of the Cowley Road Hospital, Oxford. Like the best of "follow-up" studies it is amply reinforced by necropsies. Old age represents the end-results, and for the cardiologist who is faced most commonly with rheumatic heart disease in the young or middle-aged patient the authors' demonstration of the frequency and distribution of valvular lesions among a geriatric population is most illuminating.

Dr. Bedford and Dr. Caird deal with problems which are likely to arise with increasing frequency in the future. For instance, their experience indicates that in the elderly the development of auricular fibrillation commonly precipitates congestive failure. How important is it to make a determined effort to restore normal rhythm with quinidine in the older age groups, and for how long can normal rhythm be maintained thereafter? That tight mitral stenosis is not so uncommon in old age is now established, but it is less well appreciated that the mechanical handicap thereby imposed on the elderly woman may prove less detrimental to her than a similar degree of mitral obstruction in her grandchild. In fact the exertional capacity of the old lady may improve or at least remain stationary, while her granddaughter runs into more serious difficulties.

Evidence accumulates to support the contention that aortic regurgitation may arise from causes other than destructive valvular lesions. Dilatation of the first part of the ascending aorta accompanied by degenerative changes in the arterial wall with or without hypertension is undoubtedly a cause of aortic incompetence in the elderly.

If the book has a shortcoming it is that the authors, who have concentrated so effectively on clinical problems, have not perhaps made as much use of radiology as might have been expected. More work could be done with advantage in this particular field. Not the least valuable part of the book is the well-documented list of references to current cardiological literature—a treasury of sound clinical and pathological experience, well worthy of detailed study. The book makes a real contribution to our knowledge of valvular heart disease and opens the way for similar studies in other branches of cardiology.

RAE GILCHRIST.

## DARWINISM AND SOCIETY

*Darwinism and the Study of Society. A Centenary Symposium.* Edited by Michael Banton. With an Introduction by J. Bronowski. (Pp. 191+xx. 21s.) London: Tavistock Publications. Chicago: Quadrangle Books. 1961.

The wave of centenary comment on Darwinism is now receding, and it is perhaps natural to see this symposium as a ripple in its wake. It is, however, quite a considerable ripple and contains several essays of originality and interest. The four from biologists show a more confident approach than do the eight from historians and sociologists, and this is not to be wondered at. Biology has a wide range of established disciplines to offer to the sociologists, but they, having once been bitten by so-called "Social Darwinism," are naturally cautious in their response.

The task of sweeping away the debris of "Social Darwinism" is undertaken in this symposium by Hogben. He does it with gusto, though he avoids joining in the rather undiscriminating rejection of the relevance of our animal origins and animal nature to our social behaviour that is shown by Stark in another essay. Stark resurrects and analyses a social Darwinist controversy of sixty years ago, and while he gives a

real sense of period his conclusions might be taken as a discouragement of many legitimate and rational branches of human biology.

Waddington defines the human evolutionary system and draws upon genetical experience to suggest possible analogies between biological and social inheritance. The latter is, of course, dependent upon human communication, which Barnett compares and contrasts with its animal counterparts. Maynard Smith pursues the analogical resemblances between historical and evolutionary processes, and is prepared to admit that both may obey general laws of change and that consequently the evolutionist may have something to learn from the historian's material.

In general the sociologists' essays are happier the less relevant they are to the title of the symposium. Two—on Darwin's debt to his period as a medical student in Edinburgh and on his place in the "history of ideas"—cannot by their nature add much that is new. The most considerable, by Ginsberg, is a survey of social evolution which concedes the continuity of history and evolution but finds little occasion to draw upon Darwinism in treating society.

D. R. NEWTH.

## ORTHOPAEDIC SURGERY

*Principles of Orthopaedic Surgery.* By Paul C. Colonna, M.D. Revised edition. (Pp. 799+ix; illustrated. £7 10s.) London: J. and A. Churchill, Ltd. 1960.

This is a sound review of the general principles of orthopaedics, for the most part arranged on a regional plan. With preliminary discussions of the physiology and pathology of the locomotor system, the main text is followed by a review of the neuromuscular disorders, neoplastic diseases of bone, and external surgical appliances. Each of the seventeen chapters is followed by a valuable bibliography. Apart from references to new editions of standard works relatively few original papers published after 1950 are noted. This perhaps suggests that by that year the foundations and superstructure of orthopaedics had been completed. The detail of description is at times uneven—for example, in the description of surgical approaches to the humeral shaft and the absence of any description of approaches to the femur. The illustrations of capsular repair for recurrent dislocation of the shoulder are misleading, particularly those purporting to show the Bankhart and Putti-Platt operations.

But these are minor criticisms, for the book reflects basic British–American orthopaedic practice and it will admirably serve its purpose as a text for senior students and as a guide to general practitioners, though the surgeon in training will require more than this can offer. Dr. Colonna is one of the American masters of orthopaedics. He has made great contributions to the surgery of the hip-joint, and these are here well outlined. One is left with the wish that he would produce something which would convey to the practising surgeon more of his erudition and wisdom in other aspects of the subject.

NORMAN CAPENER.

## SEXUAL BEHAVIOUR

*The Encyclopaedia of Sexual Behaviour.* Volumes I and II. Edited by Albert Ellis, Ph.D., and Albert Abarbanel, Ph.D. (Pp. Vol. I 1–574+xxii, Vol. II 575–1059+viii. £7 15s. the set.) London: William Heinemann. 1961.

Psychiatrists, physicians, surgeons, psychologists, sociologists, anthropologists, lawyers, and others have written chapters in these well-produced, well-indexed and highly priced volumes. Eighty-three of the ninety-eight authors hold appointments in the United States, and this circumstance is reflected in the sections for which each is responsible. Every aspect of sexual behaviour and kindred matters seems to be mentioned with the possible exception of nullity in marriage. In addition to well-known topics such as perversions, impotence, sterilization, abortion, prostitution, to name but a few, there are studies of different cultures showing that the diversity in attitudes toward sexual matters is linked with the prevailing social customs. Thus in African negro tribes sex life is part of a co-ordinated sociological system, whereas in Latin America there is no such co-ordination and "the sex pattern is as varied as the climate."

Many of the contributions on special subjects are of general interest: "Music and Sex," "Sexual Dynamics in Contemporary Dance," and "Censorship of Sexual Literature" are examples. The last-named gives an admirable survey of the vagaries of censorship in the British Isles, Eire, the United States, France, and other European countries.

Repetition is inevitable in a collection of monographs such as this, and the claim "that every one of the articles is original and up to date in every respect" is difficult to accept. Nevertheless the editors have done a service in assembling current knowledge on normal and abnormal sexuality in a concise form that makes reference simple. More than three years have been spent in the Herculean task of planning and producing the volumes, and the editors are justly proud of their work.

E. A. BENNET.

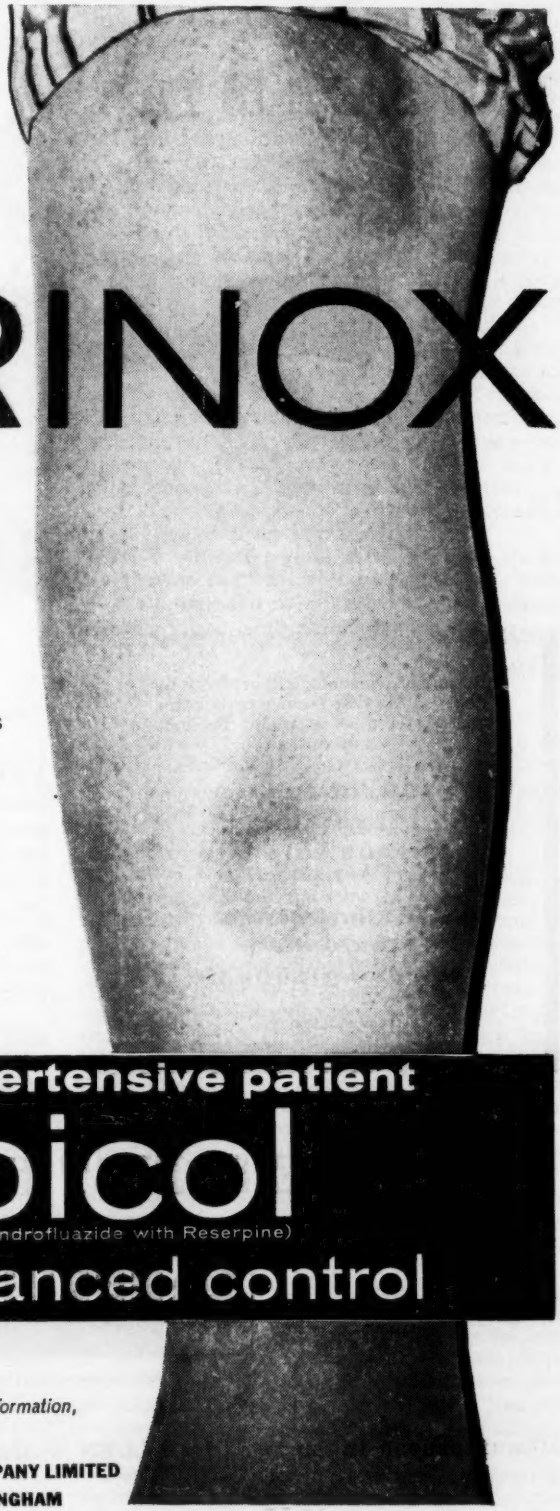
## CARDIOVASCULAR "RETRIEVAL GUIDE"

*Index-Handbook of Cardiovascular Agents.* Volume 2, Parts 1 and 2. Literary director: Isaac D. Welt. (Pp. 1,568 +lv. $15.) Washington: National Academy of Sciences, National Research Council. 1960.

When manufacturers of scientific products are faced with a problem new to them they often find it cheaper to solve it themselves than to search through the voluminous literature to discover if and how someone else has solved it beforehand. This difficulty is now being met by the preparation of what are coming to be known as "retrieval guides," in which vast quantities of published material are processed and the information in them is made accessible. The two volumes reviewed here are an example of such a guide.

They list some 13,400 scientific communications on cardiovascular topics published during the period 1951–5, each of which has been analysed page by page and annotated with reference to the various drugs involved. Future volumes will deal with the periods 1931–50 and 1956–60. Volume two thus appears before volume one. The analyses are made on I.B.M. punched cards and the typewritten material is photographed to produce the photo-offset plates from which the books are printed. The books themselves are two thick demy quarto volumes with a page of 11 inches by 8¼ inches (28 by 22 cm.). They consist of explanatory material, bibliography, author index, and subject index, the last making up about three-quarters of the two volumes.

Cardiologists and pharmacologists in general and researchers, writers of textbooks, reviewers, and librarians in particular will be immensely grateful to Dr. Welt and his fellow labourers in the Cardiovascular



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Literature Project for having undertaken this herculean task and for enabling them so easily to obtain references to the literature on any item in this field. The National Research Council of America, which finances the project, has shown how wisely the wealth of a nation can be expended and has put the rest of the medical world in its debt.

L. J. WITTS.

## THE CHEST SURGEON'S ORBIT

*Surgical Diseases of the Lung.* By Buford H. Burch, M.A., M.D., and Arthur C. Miller, M.S., M.D., F.A.C.S. (Pp. 128 + xii; illustrated. 68s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

In this short work the authors give their views on the basic pattern of chest disease which comes within the orbit of the surgeon. This is deliberately done without references, figures, or index, and within 70 pages a great deal of sound instruction and common sense is shown. It is not a book for the expert, but it should serve to tell many student doctors of the scope of thoracic surgery without confusing them with unnecessary detail.

Forty full-page radiographs of various normal and pathological conditions are reproduced at the end of the text, and though the descriptions are scant the reproduction is so good that little else is necessary.

T. HOLMES SELLORS.

## YOUNG WOMEN'S WORK

*Hospital Careers for Girls.* By Joan Llewelyn Owens. (Pp. 160. 15s.) London: The Bodley Head. 1961.

This little book will be a useful guide for young women who wish to occupy themselves in work connected with hospitals. The facts are well arranged and the text is brightened by short accounts of personal visits to departments in action. Details are given of the type of work provided, personal qualities and preliminary education required, the course of study to be gone through, the cost of and time taken by training, and the prospects open on qualification in each of eight occupations, and in the first chapter brief references are given about seventeen other types of work which are to a greater or less degree connected with hospitals.

The eight occupations of which full details are given in later chapters are those of almoners, dietetics, laboratory technicians, medicine, nursing (including midwifery), occupational therapy, physiotherapy, and radiography. This choice excludes at least one of the professions auxiliary to medicine included in recent Government legislation and does not include dentistry, in which women can do excellent work. The authoress might well consider expanding the book to give a comprehensive view of the whole question of women's careers in connexion with hospitals and medicine.

It is stated (on page 26) that there are at present about 12,000 working almoners—surely the number of *trained* almoners is very much below this? As to the title: it is commonly regarded as unwise for young women under the age of 18 to work in hospitals, so that "careers for girls" does not seem entirely appropriate. When does a girl become a young woman? Perhaps the justification for the title is that girls have to consider their future long before they start their career.

ZACHARY COPE.

## PERITONEOSCOPY

*La Laparoscopie. Son Importance en Pathologie et dans la Pratique Clinique. Notes de Technique.* By G. Lenzi, G.-B. Cavassini, and E. Lenzi. (Two volumes.) (Text: pp. 344; illustrated. Atlas: pp. 126; illustrated. 100 NF. the set.) Paris: Masson et Cie. 1960.

This French translation of an Italian book, emanating from Professor Sotgiu's medical clinic in Bologna, is a comprehensive and informative work; and whereas many articles have been published on peritoneoscopy since its introduction in 1910 *La Laparoscopie* is the only complete book on the subject known to the reviewer. Though there are some individuals in this country who practise peritoneoscopy quite extensively it is probably true to say that it is neither a common nor a popular procedure in most hospitals.

In the first of two volumes the authors give an account of the history of the operation, detail instruments and technique, and discuss fully the indications and contraindications. Combined peritoneoscopy and cholangiography is also discussed, largely to be condemned. The second volume includes many fine colour photographs of normal and diseased organs. There are also a number of colour photomicrographs of needle biopsies of the liver.

This is certainly a most useful reference work, and though some may feel that it makes much of a relatively restricted subject it should provide much information for those interested in peritoneoscopy.

R. S. MURLEY.

## THE VERSATILE COOMBS TEST

*The Anti-Globulin (Coombs) Test in Laboratory Practice.* By I. Dunsford, Ph.D., M.I.Biol., and Jean Grant, F.R.C.P. (Pp. 120 + xiii. 12s. 6d.) Edinburgh and London: Oliver and Boyd. 1959.

The anti-globulin test has now been in regular use in blood-group serology for some 15 years. Many if not most of the rather complex techniques involved in the preparation and use of anti-human-globulin serum have, however, remained available only in papers published in journals, or even in some cases only through direct communication between laboratories or by means of stencilled notes of limited circulation. There has thus been a great need for a comprehensive book on this vitally important test. This need is to a very large extent met by the work under review. Like many books dealing with fields where research is active, it was, however, published at an unfortunate moment, when considerable advances were being made which were published just too late for incorporation in the book. If, therefore, in this review the lacunae are stressed it is in the hope that they will be filled in a subsequent edition.

The theoretical and historical chapters are now somewhat out-dated by recent work on the multiplicity of antibodies present in sera prepared by the injection of human serum into animals. Most of these antibodies are of little or no consequence in relation to the anti-globulin test, but one of them, which reacts with complement, is vitally important both scientifically and clinically.

The chapter on production of anti-human-globulin serum shows evidence of much experience, but the distinction between production in rabbits and in goats

is not everywhere made clear. The chapter on processing is admirable, but that on standardization, while adequate for most purposes, does not refer sufficiently to the theoretical background. The account of the complexities of the reaction is fairly full, but omits to mention the very useful immunoelectrophoretic method of investigation, which demonstrates the complexities of the reagent used. The chapters on technique, on the causes of false reactions, and on applications of the test are almost entirely admirable, containing the fruits of much practical experience, but once again there is inadequate reference to "non-gamma-globulin" or complement-fixing antibodies and to the special techniques or even specially prepared and standardized anti-globulin sera which may be needed in investigating them. A final chapter deals with a miscellany of oddments. There is a brief but adequate index and the book is well produced.

Provided that the omissions mentioned are borne in mind the book can be recommended as a valuable practical laboratory guide, which will, we hope, run through many future editions, incorporating new work, as it appears, on this highly versatile test.

A. E. MOURANT.

## GROWTH AND THE TEACHER

*Education and Physical Growth. Implications of the Study of Children's Growth for Educational Theory and Practice.* By J. M. Tanner, M.D., D.Sc. (Pp. 144; illustrated. 12s. 6d.) London: University of London Press Ltd. 1961.

In his preface Tanner states that this book is addressed to teachers, lecturers in training colleges and university departments, and institutes of education. In my opinion all teachers and trainers of teachers will find it of great value, and I would add that all paediatricians, doctors, and intelligent laymen with children of their own would find much of interest and importance in it. The price, furthermore, is low.

The book is based on a series of lectures given to the Institute of Education at the University of Leeds. I have long felt that paediatricians and teachers have a great deal of common interest, and each can contribute much to the knowledge of the other. This work is a good example of a medical contribution to the teaching profession.

The book gives an outline of physical growth and the environmental and genetic factors affecting it. It discusses in an interesting and readable way the order and importance of the maturation of the various tissues of the body and of the mind, with some comment on the implications of this maturation to those teaching children. These include sexual differences in the rate of maturation, the relationship of psychological and intellectual development to physical maturation, the problems involved in trying to teach children of very different emotional and physical levels of maturation in one class, and the predictability of adult height from physical growth in infancy and childhood.

I liked the introductory chapter, which sets out clearly the plan and aim of the book. The summary and conclusions add to the value of this excellent volume by collecting together the main points and their implications in the realm of child management. It can be recommended without reservation.

R. S. ILLINGWORTH.

## BOOKS RECEIVED

*Review is not precluded by notice here of books recently received*

***Neurophysiology.*** By Theodore C. Ruch, Ph.D., Harry D. Patton, Ph.D., M.D., J. Walter Woodbury, Ph.D., and Arnold L. Towe, Ph.D. (Pp. 521+xi; illustrated. 70s.) Philadelphia and London: W. B. Saunders Company. 1961.

***Lésions Provoquées par les Radiations Ionisantes.*** By J. Delarue and L. Frühling. (Pp. 208; illustrated. 42 NF.) Paris: Masson et Cie. 1960.

***British Columbia Cancer Institute Vancouver Five Year Result of Treatment 1946–1954. With a Synopsis of Treatment Policy 1961.*** By A. Maxwell Evans, M.D., C.M., D.M.R.E. (Pp. 269+xv; illustrated. No price.) Vancouver: British Columbia Cancer Institute. 1961.

***Medical Services of the R.A.N. and R.A.A.F.*** By Allan S. Walker, M.D., Ch.M., F.R.A.C.P., and others. (Pp. 574+xv; illustrated. 35s.) Canberra: Australian War Memorial. London: Angus and Robertson Ltd. 1961.

***Thoracic Diseases Emphasizing Cardiopulmonary Relationships.*** By Eli H. Rubin, M.D., F.A.C.P., F.C.C.P., and Morris Rubin, M.D., F.A.C.S., F.C.C.P. (Pp. 968+xviii; illustrated. £8 15s.) Philadelphia and London: W. B. Saunders Company. 1961.

***Respiration in Health and Disease.*** By R. M. Cherniack, M.D., M.Sc., F.R.C.P.(C.), and L. Cherniack, M.D., B.Sc., M.R.C.P.(Lond.), F.R.C.P.(C.), F.A.C.P. (Pp. 403+xii; illustrated. 73s. 6d.) Philadelphia and London: W. B. Saunders Company. 1961.

***Sports Injuries and their Treatment.*** By John H. C. Colson, F.C.S.P., M.S.R.G., and William J. Armour, M.C.S.P., M.S.R.G. (Pp. 224; illustrated. 25s.) London: Stanley Paul. 1961.

***Tropical Nutrition and Dietetics.*** By Lucius Nicholls, C.M.G., B.A., M.D., B.C., revised by H. M. Sinclair, M.A., D.M., B.Sc., M.R.C.P., and D. B. Jelliffe, M.D., F.R.C.P., D.C.H., D.T.M.&H., F.A.P.H.A. Fourth edition. (Pp. 457+xii; illustrated. 50s.) London: Baillière, Tindall and Cox Ltd. 1961.

***Kliniska Och Experimentella Undersökningar Med Ekoencefalografi.*** By Brita Lithander. (Pp. 15. No price.) Stockholm: Kungl Boktr. 1961.

***Chemical and Biophysical Studies of Microscopic Structures in Compact Bone.*** By John Strandh. (Pp. 16. No price.) Uppsala: Almqvist and Wiksells Boktryckeri AB. 1961.

***Doctor on Lake Nyasa.*** By Michael Gelfand, C.B.E. (Pp. 70. illustrated. No price.) Michael Gelfand. 1961.

***Initiation à la Médecine. Six Leçons d'Introduction aux Études Médicales.*** By Henri Péquignot. (Pp. 104. No price.) Paris: Masson et Cie. 1961.

***Die Poliomyelitiscke Lähmung und ihre Behandlung.*** By Hermann Fredenhagen. (Pp. 162; illustrated. 26 Sw. fr.) Stuttgart, Basle: Benno Schwabe. 1961.

***Précis de Médecine Infantile.*** By Cl. Launay, P. Grenet, and F. Verliac. (Pp. 899+vii; illustrated. 65 NF.) Paris: Masson et Cie. 1961.

***Les Grandes Activités du Rhinencéphale.*** By Th. Alajouanine. Volume 11. *Physiologie et Pathologie du Rhinencéphale.* (Pp. 337; illustrated. 43 NF.) Paris: Masson et Cie. 1961.

***The Essentials of Paediatric Surgery.*** By H. H. Nixon, M.A., F.R.C.S., and Barry O'Donnell, M.Ch., F.R.C.S., F.R.C.S.I. (Pp. 315+xii; illustrated. 40s.) London: William Heinemann. 1961.

***Anatomie du Rhinencéphale.*** By H. Gastaut and H. J. Lammers. Volume 1. (Pp. 166+viii; illustrated. 22 NF.) Paris: Masson et Cie. 1961.

***Agression et Réanimation en Neuro-Psychiatrie.*** By R. Coirault. (Pp. 381+xxiv; illustrated. 52 NF.) Paris: Masson et Cie. 1961.

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## THE CASE OF THE PLASTIC SURGEONS

The warning notice issued by the Disciplinary Committee of the General Medical Council for the guidance of medical practitioners contains the following statement in relation to advertising:

> "In the opinion of the Committee, the practices by a medical practitioner
>
> (1) of advertising, whether directly or indirectly, for the purpose of obtaining patients or promoting his own professional advantage; or, for any such purpose, of procuring, or sanctioning, or acquiescing in the publication of notices commending or directing attention to the practitioner's professional skill, knowledge, services or qualifications, or depreciating those of others; or of being associated with, or employed by, those who procure or sanction such advertising or publication . . .
>
> are discreditable to the medical profession and are contrary to the public interest. Any practitioner resorting to any such practice is liable to erasure."

Seven plastic surgeons were last week up before the General Medical Council on the charge of advertising for patients and for seeking to profit by the publication of articles in women's magazines. The full account of the investigation in this week's *Supplement* shows that in 1954 and in 1959 articles appeared in popular women's magazines on the benefits of plastic surgery, both of them recommending application to the British Association of Plastic Surgeons for the names of specialists. The late Sir Archibald McIndoe had checked the article which appeared in 1954. In connexion with the second article a leaflet had been prepared and had been seen by the Honorary Secretary of the British Association of Plastic Surgeons. Later the editor of the journal sponsoring it was asked by the B.A.P.S. to withdraw the leaflet from circulation, and all those which had not been circulated were subsequently destroyed: approximately 2,800 had been distributed before this.

These were the principal facts before the Disciplinary Committee of the G.M.C. last week. After exhaustive cross-examination the G.M.C. committee concluded that none of the surgeons before it had advertised for the purpose of obtaining patients. The Committee at the same time expressed its serious misgiving about three points brought out in the inquiry: (1) officers or members of the B.A.P.S. had "wittingly or unwittingly co-operated in the publication in the lay press of articles calculated to stimulate members of the public to apply to the association for information about the services of plastic surgeons"; (2) the B.A.P.S. had made available the names of a limited number of plastic surgeons to persons who had applied as a result of reading such articles; and (3) members of the B.A.P.S. had been prepared to accept patients led to seek their services in this way (see *Supplement*, page 223). Though it seemed unlikely at the outset that a charge of infamous conduct would be proved against the seven surgeons, the medical profession as well as the public will have welcomed the decision of the G.M.C. as the correct one to make in somewhat unusual circumstances.

From comments made in the national press, it looks as though once again public opinion is critical of the ethical code governing the professional life of practising doctors, forgetting that such a code is designed primarily to protect the public. The grave charge of advertising having been disposed of, the question arises whether it was unwise, or indeed unethical, for lists of specialists to be sent to an inquirer and whether a patient should be obtained in this way. Evidence showed that the B.A.P.S. was not alone in this practice. From what is stated above, the G.M.C. appears to regard this as unethical—*appears*, because its "serious misgiving" and "much concern" are related to three connected events: publication of magazine articles recommending application to a specialized body; the issue to patients by this body of a limited list of specialists; the acceptance by specialists of patients introduced in this way.

In Britain the etiquette of relationship between specialist, general practitioner, and patient is that the last should go to the first through the mediation of the second. This custom is not necessarily followed in other countries or looked upon in such countries as being a breach of etiquette or of the overstepping of that ill-defined line between etiquette and ethics. But the British custom of referral of patient to specialist by the general practitioner is in the best interests of the patient. The general practitioner, being responsible for the continuing care of his patient, is the only person really fitted to advise him or her about the need for this or that treatment, because only he knows the personal and family history of such a person through direct contact and knowledge. The offending leaflet referred to in the case against the plastic surgeons recognized this by stating, "Your own doctor is the one to put you in touch with the most competent plastic surgeon for your case." But it went on to say, "There are, however, some more conservative doctors who are not sympathetic to cosmetic surgery, and yours may be

[1] Clarkson, P., and Stafford-Clark, D., "Role of the Plastic Surgeon and Psychiatrist in the Surgery of Appearance," *Brit. med. J.*, 1960, 2, 1768.

one." Then followed the advice that a list of accredited specialists could be obtained by applying to the British Association of Plastic Surgeons. As the counsel for one of the surgeons is reported to have said: "Was the giving of lists of names advertising or the response to a real need?" If, as was shown last week, the doctor is here in a dilemma, we should recognize also that the patient may be in one too. It does not require much imagination to appreciate the psychological value of cosmetic surgery, as was shown in an article published in the *Journal* about a year ago,[1] and it is not difficult to imagine that a patient wishing to have a cosmetic operation might for social reasons prefer her general practitioner to be kept in ignorance of this.

Any one breach of etiquette or infringement of ethical rules is almost bound to be followed by others. Since 1948 many people believe there has been an increase in such breaches, and some have gone so far as to suggest that now the consultant or specialist is less dependent upon the general practitioner for his patients the less careful is he about observing the unwritten as well as the written rules governing the relationship of doctors to one another and to the patients they look after. Mr. J. H. Gunlake, President of the Institute of Actuaries, last week defined a professional practitioner thus: "One who, having undergone a rigorous formal training and been tested and registered as competent at the end of it, makes and keeps a vow of high ethical behaviour in bearing personal responsibility for matters of moment." The public whom such training and ethical codes are designed to protect too often show their ignorance of this by protesting at the restrictions doctors place upon themselves. It is the formulating and acceptance of ethical codes that in addition to training distinguish the professional man from a tradesman or a technician. The ordeal of inquiry undergone by the seven plastic surgeons last week will have served at least one valuable purpose if it brings sharply home to doctors the need for scrupulous care in their relationship with each other and with the people among whom they live. They will also note, it is hoped, the trust expressed by the Disciplinary Committee that there will be no recurrence of the events especially singled out for criticism.

## DIABETES MELLITUS AND HORMONE IMBALANCE

Though von Mering and Minkowski discovered in 1899 that pancreatectomy produces diabetes mellitus in dogs insulin was not isolated until Banting and Best's achievement in 1921. We now agree that absolute or relative lack of insulin is probably responsible for the diabetic syndrome of wasting and polyuria with hyperglycaemia and glycosuria which von Mering and Minkowski reproduced in these dogs; for this acute or severe diabetic syndrome is always relieved by treatment with insulin whether in the pancreatectomized dog or in the human patient. In this acute diabetic syndrome insulin also relieves the protein wastage and its associated excessive loss of nitrogen in the urine, the ketoacidosis, and the hyperlipaemia as well as the more familiar carbohydrate disorders. But though insulin has enhanced the diabetic patient's expectation of life a number of complications are all too familiar—namely, retinopathy, nephropathy, peripheral vascular disease, and neuropathy. Clearly lack of insulin secretion is not easily made good by periodic injections or diabetes mellitus is a more complex disorder than at first thought.

We now know that the metabolism of carbohydrate, of fat, and of protein are interrelated and regulated by a balance of hormones rather than each simply by one hormone. Diabetes mellitus represents a disorder of this regulation, and involves not only lack of insulin but also an overaction of the antagonists of insulin[1]; for Houssay and colleagues[2] showed that the diabetes of pancreatectomy could be ameliorated by removal of the anterior pituitary. Further, F. G. Young[3] showed that permanent diabetes could be induced by excessive treatment with one of these antagonists, the anterior pituitary's growth hormone, probably because this leads to exhaustion of insulin production; and in his Litchfield Lecture, published in the opening pages of the *Journal* this week, Professor Young recounts his subsequent experimental research on diabetes which has grown from this observation.

Diabetes is sometimes a feature of a more complex endocrine syndrome. Then the deficiency of insulin is partly caused by excess of various hormonal

[1] See *Brit. med. J.*, 1961, **2**, 632.
[2] Houssay, B. A., Biasotti, A., and Rietti, C. T., *C.R. Soc. Biol. (Paris)*, 1932, **111**, 479.
[3] Young, F. G., *Recent Progr. Hormone Res.*, 1953, **8**, 471.
[4] Cushing, H. W., *The pituitary body and its disorders: clinical states produced by disorders of the hypophysis cerebri*, Philadelphia and London. 1912.
[5] Natelson, R. P., *Ann. intern. Med.*, 1954, **40**, 788.
[6] Stanton, E. R., Jones, H. W., and Marble, A., *A.M.A. Arch. intern. Med.*, 1954, **93**, 911.
[7] Fraser, R., and Harrison, M., in Wolstenholme, G. E. W., and O'Connor, C. M. (ed.), *Ciba Foundation Colloquia on Endocrinology*. Vol. 13: *Human Pituitary Hormones*, p. 135. London. 1960.
[8] Goldenberg, M., Serlin, I., Edwards, T., and Rapport, M. M., *Amer. J. Med.*, 1954, **16**, 310.
[9] Unger, R. J., and Madison, L. L., *J. clin. Invest.*, 1958, **37**, 627.
[10] Warren, S., and LeCompte, P. M., *The Pathology of Diabetes Mellitus*, 3rd ed. Philadelphia. 1952.
[11] Maclean, N., and Ogilvie, R. F., *Diabetes*, 1955, **4**, 367.
[12] Wrenshall, G. A., Bogoch, A., and Ritchie, R. C., ibid., 1952, **1**, 87.
[13] Slater, J. D. H., Samaan, N., Fraser, R., and Stillman, D., *Brit. med. J.*, 1961, **1**, 1712.
[14] Steinke, J., Taylor, K. W., and Renold, A. E., *Lancet*, 1961, **1**, 30.
[15] Vallance-Owen, J., and Wright, P. H., *Physiol. Rev.*, 1960, **40**, 219.
[16] Bornstein, J., and Park, C. R., *J. biol. Chem.*, 1953, **205**, 503.
[17] Vallance-Owen, J., and Lukens, F. D. W., *Endocrinology*, 1957, **60**, 625.
[18] —— Hurlock, B., and Please, N. W., *Lancet*, 1955, **2**, 583.
[19] Field, J. B., and Stetten, D., *Amer. J. Med.*, 1956, **21**, 339.
[20] Vallance-Owen, J., and Lilley, M. D., *Lancet*, 1961, **1**, 804.
[21] Antoniades, H. N., *Endocrinology*, 1961, **68**, 7.
[22] Raben, M. S., *Recent Progr. Hormone Res.*, 1959, **15**, 71.
[23] Read, C. H., and Bryan, G. T., ibid., 1960, **16**, 187.
[24] *Ciba Conference on Immunoassay*, 1962, to be published.

antagonists, which are revealed clinically by various other aspects of the syndrome. The diabetic syndrome is seen in 20–25% of acromegalics,[4 5] especially among those acromegalics with a family history of diabetes; and also in about 25% of cases of Cushing's syndrome.[6] But it can also co-exist with either anterior-pituitary deficiency or adrenocortical deficiency.[7] Less frequently it may be a subsidiary feature of phaeochromocytoma.[8]

But what of diabetes where there is no hint of any associated endocrine disease? In apparently uncomplicated mild diabetes R. J. Unger and L. L. Madison[9] found that the hypoglycaemic response to a test dose of tolbutamide was subnormal, which suggested that the insulin reserve was low but gave no clue to whether this was primary or consequent on other disorders. In apparently uncomplicated diabetes other factors have long been suspected both because the pathological changes found at necropsy in over half the diabetic pancreases are slight[10] and because diabetic patients tend to fall into one of two groups—the juvenile, thin, insulin-requiring, ketosis-liable type, or the mild, obese, older type. N. Maclean and R. F. Ogilvie[11] in their estimation of the mass of pancreatic $\beta$-cells in post-mortem material from diabetics found a smooth continuum ranging from near zero to normal values. G. A. Wrenshall and colleagues[12] found the same for the insulin extractable from these pancreases.

Assays for insulin in blood serum are being applied to this problem but give no final answer yet. Bioassays probably measure only insulin-like activity or a balance between insulin, its synergists, and its antagonists, which varies with the tissues used in the assay. Immuno-assay may not measure all the circulating insulin.[13] However, J. Steinke and colleagues[14] found that in untreated diabetics, whether of the juvenile or the obese type, an excess of insulin-like activity can be detected, while J. Vallance-Owen and P. H. Wright[15] by another method detected no insulin in the insulin-requiring diabetics but normal amounts in the obese type. This suggests that an insulin antagonist circulates in the juvenile type of the disease and that it can be detected by one method and not by the other. As Professor Young notes, insulin antagonists have been found in the circulating plasma in diabetic states of various types—in alloxan-treated rats,[16] in pancreatectomized cats,[17] in untreated insulin-requiring diabetics,[18] and especially in ketotic diabetic patients.[19] These antagonists have also been detected in small amounts in normal serum,[20] but we do not know how many different types there are. Though their presence seems dependent on anterior-pituitary and adrenal function they are not merely the hormones from these glands. Efforts are being made to define more precisely their nature and possible role in causing diabetes. Further, not only may insulin circulate bound to various plasma proteins but it may circulate in more than one form.[13 21] So here is another mechanism which, though not yet clearly defined, might become disordered in diabetes.

Professor Young shows that over-production of growth hormone could sometimes be one of the primary disorders of diabetes mellitus. In the adult the growth hormone is concerned with maintenance rather than growth, for the name merely labels an easily recognizable effect of the hormone. Among its major functions are mobilization of fat and the promotion of its oxidation.[22] Hence minor increases in secretion of growth hormone might produce no recognizable acromegaly and yet be important for the development of diabetes, a possibility suggested by Professor Young's evidence. Unfortunately the immunological assays of growth hormone[23] are subject to several errors when applied to untreated sera.[24] Consequently the results obtained with this assay in relation to diabetic complications must be taken cautiously. The effects of pituitary ablation in severe diabetic retinopathy are now being studied in several centres. They may later lead to the better management of patients with diabetes and to the prevention of the complications of this disease, even to the prevention of the disease itself.

## THE BRAIN-DAMAGED CHILD

The syndrome of the brain-damaged child has recently attracted attention. Though Dr. D. A. Pond's comprehensive discussion of it in his second Goulstonian lecture, published at page 1454 of the *Journal* this week, does not disguise the diffuseness and uncertainties of the concept its importance is undoubted. And it concerns the general practitioner as well as the specialist.

The injuries concerned may be of many kinds. They include physical trauma to the skull at birth or during the first few years of life, anoxia, encephalitis, and meningitis. But the clinical picture of the sequelae is much the same whatever the original cause. It is characterized chiefly by hyperkinesis (motor restlessness), distractibility and short span of attention, antisocial behaviour, low intelligence, and anxiety. Intellectual impairment seems to be almost invariable and plays a central part in the pathogenesis of the reaction as a whole. Hyperkinesis is especially

common in the very young, aggressiveness most prominent a little later, and anxiety more conspicuous in adolescence. Symptoms or signs which can be related to focal as opposed to generalized brain damage are less frequent in these patients; for example, psychogenic mutism is commoner than dysphasia. Environmental factors such as family difficulties seem to affect both the pattern and persistence of disability, and no doubt such considerations determine Pond's statement that the management of these cases "requires the fullest and deepest psychiatric approach." Unfortunately little reliable information is available about the future of these difficult children.

The weakness of the concept of the brain-damaged child lies in the non-specific nature of the symptoms and the uncertainty in any particular case of their relation to brain injury. The air encephalogram is too coarse a measure of brain damage to detect minor or diffuse injury; the electroencephalographic changes seen in these cases are of uncertain significance; and the psychometric tests routinely applied to young children are poorly standardized. We are thrown back on the clinical history. This furnished the only evidence of brain damage in more than half of Pond's cases, and every clinical research worker as well as every expert medico-legal witness knows the fallacies of retrospective study based on people's recollections.

As with all well-chosen subjects for annual lectures this topic raises more questions than it answers. How specific is this clinical syndrome—and how often does an identical pattern of behaviour occur as a "constitutional" phenomenon in cases with no evidence whatever of brain injury? If injury at birth is in fact a prominent factor in the genesis of this syndrome can we look with confidence to its declining in prevalence with improvements in obstetrics? What is the incidence of the condition in patients who have suffered authenticated cerebral injury during the first few years of life?—for the child's brain has remarkable powers of recuperation even after severe trauma. How far can the behaviour problems and restlessness be controlled by the impressive battery of modern psychotropic drugs? And what really happens to these problem children in the end? Retrospective studies have a limited application in fields such as this and sometimes lead to the building of a conceptual edifice which takes years to demolish. Prospective studies of consecutive births and unselected series of injuries of various kinds are needed to provide valid evidence on these difficult problems. The organization of the National Health Service brings the collection of such data within easy reach, and it may be hoped that the opportunity it offers is being taken in many obstetric, paediatric, and head-injury centres.

## MALNUTRITION IN OLD PEOPLE

Despite steadily rising standards of living, evidence of malnutrition is still to be found. The victim is almost always an old person living alone or a man with a mentally disturbed partner. Social rather than purely economic factors are usually to blame. Trouble is specially apt to arise among dietary faddists, recluses, aged alcoholics, people who are too disabled to shop and must rely on provisions which can be left at the door, and those who have no inclination to cook just for themselves or who have no knowledge of what constitutes a balanced diet. The family doctor has an unrivalled opportunity to detect malnutrition before anyone else, especially if, recognizing who they are, he is able to put these vulnerable people on his list for a monthly quasi-social visit.

It is hard to be sure of the earliest signs of undernutrition in an age group where involutional changes normally cause some loss of weight and muscle bulk, with consequent reduction in strength, and where wasting diseases are common. In severe cases of starvation the absence of fat and the muscle wasting are obvious enough, especially when the patient's former build is known. Some old people subsist on an unsatisfactory carbohydrate diet which contains sufficient calories. Here a state of relative protein deficiency may exist in which the temporal and masseter muscles among others are selectively wasted. Dependent oedema is sometimes due to protein deficiency, but for the confirmation of this estimations of plasma protein are often disappointing, for there are other factors besides osmotic pressure involved. Muscle wasting takes place, so that the level of circulating proteins may be maintained till the last moment. It is a common geriatric experience to treat a patient for widespread oedema, and after obtaining a good diuresis to discover how thin and clearly undernourished she is. This masking of undernourishment by body fluid is a diagnostic pitfall.

In the extremes of malnutrition the patient lies listlessly and appears pale, cold, and wrinkled, with sunken eyes, slow pulse, and lowered blood-pressure. Severe diarrhoea may follow, but it must be hoped that he or she will come under care long before this stage is reached. Lesser symptoms and signs which ought to be considered as possible evidence of impending malnutrition are lassitude, anorexia, depression, and apathy. The anorexia can be the cause of undernourishment and also the result of it. Some old people, because of psychological stresses, such as the feeling of being unwanted or the need to excite sympathy, refuse food and precipitate themselves into semi-starvation. Mental confusion is often evident too, but it is likely, by causing complete social incompetence, to be the reason for malnutrition rather than its effect. Mental confusion in old age is thought by some to be evidence of deficiency of vitamins of the B complex, but this is not conclusively proved, and the results of giving large doses of these vitamins have been unimpressive. Some workers have linked the common symptoms of anorexia, exhaustion, and headache with thiamine deficiency, but the specific

deficiency state of beriberi is not likely to be found. Similarly, pellagra must now be a very rare finding in these islands, though a combination of stomatitis, emaciation, and diarrhoea, with erythematous pigmentation of exposed skin and mental changes, would give cause for suspicion. Stomatitis, glossitis, and cheilosis, indicating riboflavin deficiency, are certainly to be seen among old people, and scurvy is far from rare. The latter occurs especially among old men who live alone, and earns itself the name of "bachelors'" or "widowers'" scurvy. It is also found in old people who have kept too slavishly and for too long to a restricted diet. Since most old people are edentulous bleeding gums are not to be expected, but perifollicular petechial haemorrhages and sometimes haemarthroses are seen instead. A distinction must be made between these purpuric spots and the larger ecchymoses so commonly found on the extensor surfaces of the hands and forearms in old people: these are entirely unconnected with scurvy and are of no significance. If wound healing is slow in older patients, or bedsores prove intractable even though pressure is relieved, deficiencies of protein or vitamin C may be the cause, for given the correct conditions healing in old people is as rapid as in the young. Even though avitaminoses occur in the elderly, these patients do not necessarily look undernourished, for often this is more a matter of incorrect than of insufficient feeding. Conversely, those who are very wasted from inanition may show no evidence of vitamin deficiencies. Iron-deficiency anaemia is common in old people but often missed; it can be evidence of general malnutrition.

More research is needed on nutritional states and even on height, weight, and build in old people. The range of normality is likely to be wide. Meanwhile the recognition of malnutrition remains a matter for clinical judgment in the light of the prevailing social circumstances. It is clearly of great importance that it should be recognized if suffering, disease, and unnecessary hospital admission are to be prevented. But it is worth bearing in mind also that many very old people are spare of build, have long been so, and may be entitled to attribute their longevity to this very fact. Obesity is also an example of malnutrition in the wider sense, and it is a more widespread cause of morbidity in the aged than undernutrition is.

## LIFE FROM SPACE?

The possibility that the fossilized remains of living organisms from another planet have been found on the earth is suggested by recent work from the U.S.A.[1] Dr. G. Claus, of New York University Medical Centre, and Professor B. Nagy, of the Department of Chemistry, Fordham University, New York, examined some meteorites which had been collected from such widely scattered localities as Southern France, Central Africa, Mighei in Russia, and Murray in the U.S.A. The meteorites were of a rare kind known as carbonaceous chondrites and they have for some time excited attention because they have been found to contain water, said to have been shown by isotope studies to be of extra-terrestrial origin, and a small proportion of organic matter. They are mainly composed of bituminous matter which has never been at a high temperature, so there is no reason why any fossil-like organism in them should not retain its original substance, scarcely altered since it died. Claus and Nagy are now reporting that they have found structures in chondrites which bear some resemblance to aquatic algae known on earth. They conclude: "We are of the opinion that these observations suggest that the organized elements may be microfossils indigenous to the meteorite."

Alternative explanations are that these structures are not the remains of living organisms or that, if they are, then the organisms reached the meteorites on the earth. Claus and Nagy naturally considered these possibilities and set out a number of arguments against them. But further work is needed to substantiate their thesis. In particular the photographs accompanying their report, no doubt owing to technical difficulties, are not of a kind that can provide an immediate confirmation of the text. A possibility to be considered is whether the bodies they found might be purely inorganic in origin. Iron oxide and other substances are known, for instance, to be the cause of concretions in rocks that can assume cell-like forms. Could such inorganic concretions form in a bituminous matrix? As to the possibility of contamination from the earth, Claus and Nagy point out that their meteorites had been kept in the dry atmosphere of a museum and "they were outdoors for only a few hours after they had fallen," yet algae require a continuously moist environment to develop. Moreover, these bodies are said to differ somewhat from algal forms known on earth.

Thus we are presented with a fascinating hypothesis to account for some rather life-like bodies found in meteorites. Whether they are indeed intimations of life beyond our planet or have a more mundane significance needs further work to decide.

[1] Claus, G. and Nagy, B., *Nature (Lond.)*, 1961, **192**, 594.

## VENTRICULAR SEPTAL DEFECT

It is generally recognized that the outlook for patients with large ventricular septal defects is poor unless the defect is closed surgically. Repair is usually possible with a fairly low operative mortality. As the disease has such an unfavourable prognosis, it might be supposed that the natural history is of remorseless and progressive pulmonary hypertension accompanied by sclerosis of the pulmonary arteries. If this view were correct it would be a powerful argument in favour of the earliest possible diagnosis and surgical correction of the defect. A recent paper from the Cook County Children's Hospital in Chicago by B. M. Gasul and others[1] suggests that pulmonary hypertension may not always be progressive in children under 2 years old. Thirty-two patients were studied by serial cardiac catheterization over a period of one to seven years. At the time of the first catheterization twenty of the children were under 2 years old and only two were

over 6. At the second catheterization there had been a decrease in the pulmonary-artery pressure in sixteen children, an insignificant change in fourteen, and a rise in only two. Gasul and his colleagues divided these patients into three groups. A group of three patients had a pulmonary-artery systolic pressure of less than 30 mm. Hg with a small left-to-right shunt. None showed any worsening of the situation two to seven years later, and one of them had no evidence of a left-to-right shunt at the second investigation. The systolic murmur had also decreased considerably in intensity in this patient. The second group comprised twelve patients with an initial systolic pressure between 30 and 60 mm. Hg but who had an average pulmonary blood flow three and a half times the systemic flow. Ten of these twelve had a lower pulmonary-artery pressure when recatheterized two to four years later, and the average size of shunt had decreased to half its initial value. The third group had pulmonary-artery systolic pressures of over 60 mm. Hg, and in this group the mean pulmonary pressures and flows did not change significantly.

The tendency of the pulmonary-artery pressure to fall in the children under 2 years old at the time of the first catheterization may have several explanations. The Chicago group postulate that the heart may outgrow its defect so that the hole is smaller relative to the heart size in the older children. They also speculate that a slow regression of the foetal type of pulmonary vasculature leads to a fall in the pulmonary vascular resistance. It is of considerable interest that four of their patients developed infundibular pulmonary stenosis with a significant pressure gradient between the body of the right ventricle and the pulmonary artery. This too decreased the size of shunt and protected the lungs from the high pressure in the right heart.

A small to moderate fall in pulmonary-artery pressure after the first year of life in some infants with ventricular septal defect has also been described by D. F. Downing.[2] The chief importance of these results is in relation to the timing of surgical intervention. Further evidence is needed particularly about the physiological variation of pulmonary-artery pressure and shunt flow in infants with uncomplicated ventricular septal defects, but if technical problems of operation in infancy remain no great harm may come from delaying surgery until a child is older.

## TRAINING OF HEALTH VISITORS AND SOCIAL WORKERS

The Health Visitors and Social Workers Training Bill, which had an unopposed second reading in the House of Commons on November 24, is a belated effort to give effect to the recommendations of two working parties set up some years ago. Both the Jameson working party on health visitors,[1] which reported in 1956, and the more recent Younghusband working party on social workers[2] called for central training bodies in their respective fields. Unfortunately the opportunity was missed initially to have the functions of these obviously closely interlinked professions examined by a single body, and even after careful study of the two reports the reader is left in some doubt about the line of demarcation between the functions of "general purpose social workers" and health visitors. It is therefore interesting that the Health Departments, after conducting two entirely separate inquiries, have now decided that the proposed two National Training Councils are to be linked to a certain extent. This may partly be due to a desire to reduce the administrative costs of the secretariats, but the Government's delayed recognition of the fact that the two fields of training should not be isolated from each other is borne out by the fact that both bodies will have the same chairman, who will be appointed by the Privy Council. Sir John Wolfenden has already been named as the first head of both Training Councils. Also some of the members nominated by local authority associations must serve on both councils, and it is to be expected that the same will apply to some of the appointments which the Ministers concerned will make themselves. In moving the second reading of the Bill Miss Edith Pitt, Parliamentary Secretary to the Ministry of Health, remarked that its shortness was not a measure of its importance.[3] She concluded: "Although the Health Service Acts and National Assistance Act were passed more than ten years ago, the aims of these Acts are not capable of full achievement without the passing of this Measure."

The Health Visitors Training Council will consist of 29 members besides the chairman: out of 13 appointed by the Health Ministers, 10 will represent the interests of health visitors and nurses, and three will be appointed in consultation with the British Medical Association and the Society of Medical Officers of Health. Another seven members appointed by the Ministers of Health and Education will represent universities and other training bodies. The remaining members will be nominated by the employers—that is, in the main, by local authorities. The slightly larger Social Workers Training Council will have a similar composition, but only two members of this body will be appointed after consultation with the British Medical Association and the Society of Medical Officers of Health. Both Training Councils are to promote and approve courses of basic and further training, arrange examinations, and initiate or support research into training. The Social Workers Training Council will concern itself in the first instance only with workers in the health and welfare services of local authorities, and it will probably concentrate on the "general purpose social worker," while the universities will remain responsible for the top stratum of "professional" social workers.

One omission in the National Health and National Assistance Acts is remedied in the new Bill. Local health and welfare authorities will at last be empowered to initiate research in their own spheres of interest under these two Acts and will thus come into line with the hospital authorities, which have been entitled to do so since July, 1948.

[1] Lynfield, J., Gasul, B. M., Arcilla, R., and Luan, L. L., *Amer. J. Med.*, 1961, **30**, 357.
[2] Downing, D. F., *Amer. Heart J.*, 1959, **57**, 669.

[1] *An Inquiry into Health Visiting*, 1956, H.M.S.O., London. See *Brit. med. J.*, 1956 **1**, 1413.
[2] *Report of the Working Party on Social Workers in the Local Authority Health and Welfare Services*, 1959, H.M.S.O., London. See *Brit. med. J.*, 1959, **1**, 1399.
[3] *House of Commons Official Report*, November 24, 1961.

# IMMUNIZATION AGAINST MEASLES

## INTERNATIONAL CONFERENCE IN WASHINGTON

[FROM A SPECIAL CORRESPONDENT]

The Paediatric Department of the University of Colorado sponsored a conference last month in Washington to consider immunization against measles. The Conference added to the information on this subject recently reported in the *B.M.J.* (November 11, pp. 1244–1253). It was attended by doctors from over 20 countries, who in the opening session discussed the prevalence and severity of measles in many different areas of the world.

### Global Prevalence and Severity

In India measles is an important cause of death, and more serious and widespread than diphtheria. In Chile the mortality is higher in the less prosperous temperate areas than in the warmer parts of the country. The disease is common and severe in certain mountainous areas of Yugoslavia where economic development is retarded. From Nigeria came a report that measles is one of the major hazards of childhood, not infrequently precipitating kwashiorkor; the case mortality for measles was believed to be 5%, with a mortality of over 20% amongst children with severe complications requiring admission to hospital. In the U.S.A. there has been a steady decline in the death rate from measles, but it is responsible for more deaths than any of the other acute infectious diseases of childhood. Even more serious is the mental defect following measles encephalitis. An abnormal slowing of the E.E.G. was present in 50% of children during the acute stages of the disease, and in an unknown but small percentage of children this finding persists. Serological studies on blood collected from many areas of the world were reported; these showed that there are few communities unaffected by measles. They also confirmed the findings of clinicians that in some crowded areas in the developing countries measles is primarily a disease of infancy and early childhood.

### Field Trials of Vaccines

Dr. J. F. ENDERS, Chief of the Research Division for Infectious Disease at Boston Children's Hospital, described the steps that had led to the isolation of the attenuated Edmonston "B" strain. Serological tests had shown that the virus of measles was related to that of distemper and rinderpest, but unfortunately hopes of using these viruses to immunize children against measles had not been fulfilled. A number of measles vaccines had been investigated in the field to protect children against the disease. These are briefly described in the Table.

| Description of Agent | Antibody Response | Results of Field Trials |
|---|---|---|
| Edmonston attenuated "B" virus alone | Good: similar to measles | Seven to 11 days after inoculation 30% of children get fever 103–105° F. (39·4–40·6° C.) lasting 2–3 days (as compared with 90% in true measles lasting 5–7 days). A mild rash occurs in 60% of inoculated children, but cough and catarrh are uncommon |
| Edmonston "B" virus with gamma globulin | Good: similar to measles | Extensive trials in the U.S.A., with smaller trials in Israel and Nigeria, have involved over 10,000 children. Only 14% have fever over 103° F. (39·4° C.); rash and other symptoms are uncommon. Encephalitis has not occurred. This combination gives over 90% protection to children later exposed to measles |
| Further attenuated strains | Probably good | Early reports on two strains were given. A strain from Russia required three injections. A more hopeful strain from America gave a good serological response and only a slight clinical reaction. At the time of the conference, trials had been completed on less than 100 children |
| Killed vaccine | Uncertain | Early trials with a killed vaccine were unsuccessful. With new methods of concentration, the development of a more effective immunizing agent based on killed vaccine seemed possible |

### Added Hyper-immune Serum

From the above Table it is apparent that the use of the Edmonston "B" strain, with a simultaneous injection of 40 units of immune serum per pound (0.45 kg.) of bodyweight, is the only tested and acceptable method of immunizing against measles available at the present time. In the U.S.A. there are considerable quantities of commercially produced hyper-immune serum (gamma globulin) available; this, however, varies in its measles-antibody titre and will require standardization. It is produced not only from blood but also as a placental extract. American practitioners frequently use hyper-immune serum in attenuating measles in normal children; for this purpose larger quantities of serum are required than when the serum is combined with vaccine. The combination of measles vaccine and hyper-immune serum has been safely and successfully inoculated into children suffering from asthma, severe congenital heart disease, sickle-cell disease, protein malnutrition, and many other conditions. The only contra-indication at the present time is leukaemia; if used in this condition there is a chance that a giant-cell pneumonia will develop.

The conference felt justified in hoping that a reliable method of immunizing against measles, likely to be of particular value in the developing countries, would become generally available within the next two years.

# JAMES MACKENZIE AND GENERAL PRACTICE TO-DAY

## EIGHTH JAMES MACKENZIE LECTURE

"To achieve the aim of medicine it is necessary to recognize disease and understand all the phases of its life history. It is evident that only one class of individual has the opportunity for acquiring this knowledge, and he is the general practitioner." This remark of James Mackenzie's was stressed by Dr. ANNIS GILLIE when she delivered the College of General Practitioners' Eighth James Mackenzie Lecture at B.M.A. House on November 25.

### Outline of Mackenzie's Life

Dr. Gillie first described Mackenzie's early life before he went into general practice in Burnley in 1878. There he spent the next 28 years, and there almost the whole of his research into the problems of the failing circulation and referred pain were carried out—and this while he was undertaking major surgery and midwifery as well as the other duties of a general practice. The success of his move to London in 1907 is well known. Among the projects initiated by him was the unit to investigate "soldier's heart" at Mount Vernon, which was set up during the first world war. In 1918 at the age of 64 he moved north to St. Andrews in Fife, where he hoped to study the health of the population and the development of disease. But severe angina pectoris drove him back to London in 1924, and he died there in 1925 from a massive coronary infarct.

### Mackenzie's Lessons for Us To-day

Many features of this great man's work were familiar, Dr. Gillie went on, but she had tried to throw light on those aspects of it that were of particular interest to the general practitioner.

The fact that he could initiate, carry through, and publish his researches on the action of the heart during the years in general practice from 1878 to 1907 was a magnificent stimulus to them all. That alongside this detailed work on the circulation he conceived and applied the doctrine of viscerosensory and visceromotor reflexes, never losing full awareness of his patients' needs in the whole field of discomfort and disease, made his researches greater still. The continuity of his work, his power of sustained thought throughout interruptions (and he was particularly fond of midwifery), were remarkable. His method of working to a hypothesis and rejecting it when facts disproved it was an example to any who struggled in the fields of clinical observation.

The principles on which he worked were set out in the introduction to *Symptoms and their Interpretation*, and again in *The Future of Medicine* published 10 years later in 1919. This book began: "To be successful in any endeavour it is necessary to have a clear idea of the object towards which we strive." In the 35 years since his death, though much had been achieved, these opening chapters still stood as admirably sound advice to those who undertook clinical and human ecological investigation.

### Crossing the Gulf

Mackenzie demonstrated, too, the value of work achieved by a team of doctors working on patients to a well-designed and well-defined plan. The College of General Practitioners had pursued these lines from the very beginning of its schemes of research. If the lone research worker of outstanding quality was rare the team of workers willing to co-operate was a system available to very many.

Mackenzie's achievement in crossing the gulf from family to hospital practice was less spectacular in his own lifetime than it would be to-day. Future opportunities were now under consideration. His professional life remained a model to be studied by reason of the way he made the change, and the difficulty that he gave himself in choosing to do so only at the highest level.

Then, too, Mackenzie demonstrated as few if any others have done the importance of listening to the patient and evaluating the evidence that only the patient could provide. He was well aware of the somatic expression of psychological unease, and valued it as an expression of dysfunction of the body. He applied this in the work on the soldier's heart. With his exactness of study of cardiac arrhythmias and of the significant and non-significant alterations in heart sounds he was able to release from the shackles of fear and of invalidism those with functional symptoms only.

His writings on the value of the viscerosensory and the visceromotor reflexes in elucidating the causes of the patient's symptoms were a superb study for the family doctor. Though much had been incorporated into routine technique in examination along these lines one could still read the first edition of *Symptoms and their Interpretation* with stimulus and refreshment.

### Medical Education

On medical education he held pronounced views. He would have been one of the first to support the College of General Practitioners, and would have approved the recent resolution of the British Medical Association that some awareness of general practice was of value to the medical student whatever section of the profession he planned to work in. The value of general practitioners both as critics of and advisers on the curriculum and as teachers was clear to him.

He was an enthusiast for extended teaching of physiology so that students should start their clinical work with a full appreciation of normal function, and he advocated the attendance of physiologists during ward teaching. He was critical of therapeutics throughout his publications and ahead of his time in criticism of the current prescribing. He urged "the recognition of the diseased state before it has produced gross structural change, and the condition that predisposed to or induced disease," and claimed that senior staff and all facilities for investigation should be available in out-patient departments. This was the exception in the 1920's but had become the rule to-day. He would be satisfied, too, by the growing practice in medical schools of supporting the attachment of students to selected general practitioners.

He might have put out a warning to-day that postgraduate study was not an end in itself but only a means for stimulating, not for satisfying, the inquiring and critical mind of the true postgraduate student. Facts and accumulated information could clog unless questioned.

### Importance of Prognosis

His endless insistence on the importance of prognosis was valuable to us to-day. "The nature of the early symptoms and the prognosis of disease are amongst the least understood matters in medicine," he wrote, and this was the backbone of his work in cardiology and of his continuing interest in pain as a symptom. Prognosis represented to Mackenzie an intellectual discipline, an exercise of judgment, by which a doctor could ultimately determine the correctness of his observations and conclusions. He believed it to be above all a duty owing to every patient that he or those responsible for him should be informed of the prognosis of his disability, acute or chronic. To-day, Dr. Gillie believed, Mackenzie's criticisms would still hold. It was of interest that complaints, whether brought to the civil courts or within the framework of the National Health Service, referred more often to errors in prognosis, to mistakes in estimating the significance of symptoms or signs, than to mistakes in diagnosis.

The College was fortunate indeed to have chosen as an ideal the life and work of James Mackenzie. The more Dr. Gillie had read of his own writing and what was written about him, the more pertinent it seemed to general practitioners' daily work and to their planning as a group. In the years since he died some of his ideals had been fulfilled. They planned that work done by the College, individually and in the fullest co-operation, might fulfil them still further.

She said that they could delight especially in the answer that he gave to some visiting physicians from the United States. During the discussion of a particular patient of his in the Burnley years, an American—puzzled, perhaps, by Mackenzie's intimate knowledge of the circumstances—asked at what point he had been called in for consultation. Mackenzie turned to him in surprise, saying, "I was never called in, I was the family doctor."

## COLLEGE OF GENERAL PRACTITIONERS

### NINTH ANNUAL MEETING

The annual general meeting of the College of General Practitioners was held at B.M.A. House on November 25. About 200 members and associates attended. Dr. ANNIS GILLIE, chairman of council, presenting the annual report, described the College's progress during the year. In the spring the Board of Trade had approved the incorporation of the College. After nearly three years' work by the awards committee, and especially by its chairman (Dr. G. F. Abercrombie), the College had received a grant of arms from the College of Arms (see *B.M.J.*, November 18, p. 1372). The appeal had progressed, largely through the personal efforts of Sir Harry Jephcott and Dr. Glyn Hughes (chairman of the appeal committee); nearly £400,000 had been received or promised.

The work of the 36 faculties of the College had been energetic and enterprising, and an increasing number of

general-practitioner symposia were being arranged each year. The New Zealand Council's arrangements for the Section of General Practice of the B.M.A. Annual Meeting in Auckland had been a great success.

### Research

A Research Foundation of the College had been formed with Sir Harry Jephcott as chairman of its board. The members included Lord Cohen of Birkenhead, Lord Nathan, the president of the College, the chairman of council, the chairman of the research committee, the hon. treasurer, and Dr. G. I. Watson. Dr. E. V. Kuenssberg, who had worked so hard as chairman of the committee which had launched this important project, was its honorary secretary. The terms of reference of this board were "to encourage general-practitioner research" in all its stages, especially that which could not be carried out easily in a laboratory or hospital, or was entirely confined to general practice. When applications were made to the board it would give a grant from its own income, or recommend to the council of the College that additional money should be made available, or it would endorse the project as worth while and support an application for a grant from other bodies. The board was anxious to receive applications about research projects, particularly in their early stages. During the year the research committee of council had been more vigorous than ever. Two major studies—on diabetes (under the direction of Dr. D. L. Crombie) and on chronic bronchitis (under Dr. John Fry)—had been completed. The activities of the Epidemic Observation Unit had been expanded. The College's register of congenital abnormalities was the largest and most comprehensive in existence, and the research register had proved to be most valuable.

### Equipment, Premises, and Education

The practice equipment and premises committee (and especially Dr. G. S. Adams, its honorary secretary) had been active in advising on practice arrangements; the summary card and other cards had had a wide distribution. The library committee offered growing service to members, and the free photocopying service was responding to increasing demands. More medical schools were represented among the Public Welfare Foundation prizewinners. The medical recording service and sound library, under Drs. John and Valerie Graves, had maintained its remarkable success.

### Elections and Presentations

Dr. G. F. ABERCROMBIE was unanimously re-elected president for 1961–2. The Foundation Council Award was presented to Dr. W. N. PICKLES. Dr. ERIC TOWNSEND was presented with the Butterworth Gold Medal for 1960–1 for his essay on "Future Trends in General Practice," and Dr. J. A. PRIDHAM received the second prize. Sixteen Upjohn travelling fellowships (up to £200 each) were awarded and Public Welfare Foundation prizes (£40 each) were presented to six final-year medical students.

### Examination in General Practice

After a full debate, in which 35 members and associates took part, the following resolution was passed by 126 members' votes to 15:

"That an examination in general practice be introduced as one of the criteria to be taken into account by the Board of Censors in considering applicants' requests for admission to membership of the College."

An announcement about this examination will be made later. It will not be held next year. Other matters concerning the by-laws, general meetings of the College, and the work of the Board of Censors were discussed. Members of the council for 1961–2 were appointed.

## ANIMAL EXPERIMENTS AND PUBLIC OPINION

### RESEARCH DEFENCE SOCIETY

"On Taking Account of Public Opinion" was the subject of the thirtieth Stephen Paget memorial lecture delivered before the Research Defence Society on November 21 by Sir HUGH LINSTEAD, M.P. The lecture was at University College, London, with Lord HALSBURY in the chair.

### Force of Irrationality

Sir Hugh Linstead said he was acting, up to a point, as *advocatus diaboli* in defence of irrationality, and after a sparkling analysis of the vagaries of public opinion, as typified by its reactions to capital punishment and flogging, he went on to consider the role of the scientist in guiding public opinion in the fields where science and politics interact, and the special area which most concerns the Research Defence Society—the use of animals for medical and surgical research and in the preparation and control of medicines.

It was a field, he said, in which there had been great controversy, though to-day this was less than in the past. That the activities of the anti-vivisection societies had become increasingly less harmful to the development of medical science was almost certainly due to a wide understanding among the public of the objectives and results of experiments involving the use of animals. In this educational process the Research Defence Society had played a distinguished part. The story itself had won acceptance by its own overwhelming cogency. The mental image of the suffering animal by which the anti-vivisectors sought to win the support of public opinion was to-day being replaced in the public imagination by the image of the child restored to health or protected from harm. The onus of proof, however, still lay on the research worker using animals to show that the balance of advantage lay heavily on the side of his experiments.

In the controversies that surrounded experiments on animals many of the facts were there for all to see in the Registrar-General's Morbidity Statistics and in the Annual Reports of the Chief Medical Officer of the Ministry of Health. But a greater part of the controversy hinged upon considerations removed from statistics. When one examined a representative sample of anti-vivisectionist literature one was almost awed by the power which could be exerted by illogical argument and selective statistics when they were reinforced by savage indignation. The arguments might be worthless and the conclusions indefensible, yet one felt that behind them and in spite of them there was a driving force independent of fact and argument yet not to be ignored. We should be hard put to explain why the sight of cruelty to animals moved us, but it was a feeling shared by many millions of people. And it was here that the real strength of the anti-vivisection campaign resided, and it was here that public opinion could most readily be rallied to support them.

### Sign of Unquiet Conscience

Public opinion might not be able to say why it reacted sharply to the death of a hunted stag caught by hounds or of monkeys in transit from India, but react it did and that reaction was as much to be taken into account in politics and in social life as any more rational phenomenon. It was the outward and visible sign among civilized people of an unquiet conscience. It might be that the public were trying to have it both ways. Probably they were. They were human. They wanted the startling benefits that had come from the use of polio vaccine without the nagging thought that they must be bought at the price of importing plane-loads of monkeys from India. But it was not a bad

(*Continued at foot of next page*)

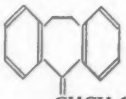
# To-day's Drugs

*With the help of expert contributors we publish below notes on a selection of drugs in common use.*

**Amitriptyline Hydrochloride**

"Tryptizol" (Merck Sharp and Dohme).

*Chemistry.*—Amitriptyline is 5-(3-dimethylamino-propylidene)-dibenzo cycloheptadiene hydrochloride. It is a white crystalline compound readily soluble in water.



$CHCH_2CH_2N(CH_3)_2HCl$

*Pharmacology.*—The effects of amitriptyline are similar to those of imipramine, and like the latter it is not a monoamine-oxidase inhibitor. Compared with imipramine it has a stronger anticholinergic and antihistaminic action but causes less potentiation of norepinephrine.

*Therapy.*—The drug is supplied in tablets of 10 mg. (grey blue) and 25 mg. (yellow). Ampoules of 10 ml., each ml. containing 10 mg. of amitriptyline hydrochloride, are also available for intramuscular use.

Amitriptyline is of value in depressive disorders, and as it has a sedative as well as an antidepressive effect it is particularly indicated where agitation, anxiety, and irritability are also prominent. In common with other antidepressive drugs it is symptomatic in action and is less effective in very severe depressions than E.C.T. A dosage of 25 mg. three times a day is usually adequate but may need to be increased in more severe cases, though not beyond a total dosage of 150 mg. daily. An initial drowsiness, which may be considerable, usually wears off but may sometimes necessitate temporary reduction in dosage. In older subjects this drowsiness tends to be more common and in them it is wise to start with a lower dosage using the 10-mg. tablets. The sedative effect is often noticeable immediately or within a few days, but one to two weeks may be required for the elevation of mood to occur. If no benefit is obtained after three weeks' treatment there is probably little value in continuing the drug.

Unlike the amino-oxidase inhibitors amitriptyline is quickly excreted and if ineffective can therefore be followed immediately by treatment with other antidepressive drugs. It may also have less tendency to activate latent schizophrenic reactions.

*Side-effects.*—The commonest side-effect is drowsiness. Other side-effects are similar to those of imipramine, though usually less severe, and include dryness of the mouth, constipation, nausea, heartburn, headaches, and increased perspiration. Oedema and paraesthesiae of the limbs occasionally occur but tachycardia and hypotension are uncommon. Jaundice and blood dyscrasias have not been reported.

*N.H.S. Basic Price.*—10-mg. tabs., 100 for 21s.; 25-mg. tabs., 100 for 42s.

(*Continued from previous page*)

thing that the public conscience should be tender on that account, for it meant that those most directly concerned were themselves kept alert to their responsibilities.

The public wanted the assurance that those who were handling animals over the wide range of experiments which in total were so beneficial to mankind were not deficient in the qualities of sensitiveness and humanity. Ultimately, said Sir Hugh Linstead, the public must rely on the personal integrity of the men and women who did this work as the safeguard against undesirable practices. Nothing could take its place.

# Correspondence

*Because of heavy pressure on our space, correspondents are asked to keep their letters short.*

## Undiagnosed Diabetes

SIR,—Interest has been aroused in the possibilities of disclosing as many as possible of the undiagnosed diabetics (possibly as numerous as known diabetics in the population) so that efforts can be made to halt the progress of their diabetes and to avert or delay diabetic complications (November 18, p. 1351). The College of General Practitioners has recognized the important role of the family doctor in the diagnosis of this early, often asymptomatic diabetes, and has organized a successful detection drive in Birmingham. Dr. I. H. Redhead[1] pioneered the use of "clinistix" in diabetes detection in general practice and concluded that much good could come from the regular testing of the urine of all patients attending the G.P.'s surgery for consultation, regardless of their complaints. He managed this in often difficult conditions, whereas less effort has usually been expended on detection under considerably more favourable conditions in general hospital wards. The consultant in charge often assumes that tests for glycosuria are conscientiously performed on his patients, but in many cases would be dissatisfied with the results actually achieved. When such tests are done the ward routine seems to involve saving and testing the first specimen passed in the morning—a time least likely to show diabetic glycosuria.

It was felt that a short trial of diabetes detection should be done in a general hospital, using simple methods. This was undertaken, starting in May, 1961, in Maryfield Hospital, Dundee, with the approval of the consultants involved. We moved from Dundee in October and have therefore to be content with the data obtained over a period of only four months. Each ward sister was interviewed and given a routine schedule of the procedure. A two-hour post-prandial urine was to be collected from each new patient and tested with clinistix and "clinitest." The result was to be recorded in the admission book rather than in a separate sequestrated urine book. If either clinistix or clinitest results were positive a one-hour post-prandial venous blood sugar was to be done. Figures above 140 mg./100 ml. at one hour or 120 mg./100 ml. at two hours were considered to indicate diabetes, since the carbohydrate contained in the preceding meal was usually less than 45 g. in a fairly slowly absorbed form, and the glucose oxidase method was used for sugar estimation. Children were excluded, as it is known that diabetes in them does not long remain asymptomatic. Results were collected each week in each ward by one of us.

| Ward | Number | Known Diabetics | New Diabetics | Other Glycosurics | No Blood Sugar Obtained |
|---|---|---|---|---|---|
| Medical men .. | 321 | 18 | 5 | 22 | 2 |
| ,, women | 354 | 31 | 6 | 15 | 3 |
| Surgical men .. | 216 | 4 | 0 | 8 | |
| ,, women | 229 | 3 | 1 | 3 | 1 |
| Obstetrics and gynaecology | 1,168 | 1 | 0 | 26 | 6 |
| Geriatric men | 86 | 1 | 0 | 0 | |
| ,, women | 125 | 9 | 0 | 3 | |
| Psychiatric men and women | 125 | 0 | 0 | 5 | |
| | 2,624 | 67 | 12 | 82 | 12 |

The results obtained are given in the Table. They illustrate that the overall incidence of known diabetes was 2.55%, and of newly diagnosed diabetes 0.46%. A high proportion (over one-third) of the hospital admissions consisted of young women coming to the maternity wards, so that the average age of the women was significantly lower than that of the men. The incidence of known diabetes in the men was 3.4%, with 0.73% newly diagnosed diabetics. In the medical, surgical, geriatric, and psychiatric wards the incidence of known diabetes mellitus in women was 5.6%, with 0.9% newly diagnosed diabetics. There was only one known diabetic in the 1,168 obstetric and gynaecological admissions and no new cases.

The conduction of this trial appeared not to tax the hospital staff, but received a varied response amongst the sisters. One sister, for instance, found only one instance of glycosuria among nearly 400 patients, whereas another sister, dealing with an almost identical population, discovered 18 glycosurics in 344 patients. It has been shown, as in previous reports, that "other glycosurics," probably mainly renal, were commoner in the men than in the women. If more thorough investigation, such as intravenous dextrose-tolerance tests, had been performed on the "other glycosuria group" it is very likely that further cases of diabetes would have been disclosed. We feel that if such a simple schedule of diabetes detection were carried out as a routine in all hospitals, preferably under the general supervision of a physician interested in diabetes, many new diabetics would be discovered at a stage when dietary or sulphonylurea treatment would usually be able to postpone or even avert the onset of symptomatic diabetes and its complications.—We are, etc.,

Department of Materia Medica and Therapeutics, University of Aberdeen.
J. M. STOWERS.
P. D. BEWSHER.

REFERENCE

[1] Redhead, I. H., *Brit. med. J.*, 1960, **1**, 695.

## G.P. Maternity Beds

SIR,—Mr. J. Vincent O'Sullivan's article (November 18, p. 1349) must interest everyone wishful to see the general practitioner take his rightful place in hospital midwifery. Mr. O'Sullivan is fortunate to obtain the consent of the practitioners to the routine examination of their booked patients in the later weeks of pregnancy by a consultant or senior registrar; but is the 36th week (postulated when contracted pelvis was common) the ideal time? Insistence on expert anaesthesia, long ago found to be so vital to the Newcastle Flying Squad, is wise indeed, as is also routine paediatric service.

Is it, however, wise to permit *x*-ray examination of the pregnant woman without consultant opinion? And is it right that the bookings should be left entirely to a sister, however senior? "A representative panel" is recommended in the Cranbrook Report[1] and supported by the Newcastle regional advisers. What criteria for booking are adopted? That more than half the patients are primigravidae is arresting. How many were over 30 years of age? Are "hospital priority" cases booked into general-practitioner beds because they are "covered" by consultants called in when he (the practitioner) deems it necessary? The list of abnormalities (post-partum haemorrhage, manual removals, late toxaemias, surgical inductions, forceps, and caesareans) is impressive, but can this be regarded as the proper use of general-practitioner beds?

Kingston is probably fortunate in the quality of its general practitioners and its good housing conditions, but what of those areas less blessed? The scheme is certainly enterprising and demonstrates how a general-practitioner unit adequately integrated with a consultant hospital can show excellent results and at the same time keep the general practitioners up to date in advances and techniques I pose my questions, however, because I feel it would be unfortunate if the Kingston scheme were regarded as a prototype for the many general-practitioner units less fortunately placed.

Surely a scheme more rational and more likely to fit into the ultimate pattern of a sound maternity service is the allocation of an appropriate number of beds, in the wards of the hospital or department (and not segregated), to general practitioners for patients regarded, after careful antenatal scrutiny, as "normal." Parallel with this an agreed number of interested general practitioners can be selected on application as "clinical assistants" in the consultant hospital or department, for periods of one year, renewable in suitable cases, on a sessional basis. Some of this latter group can be of junior trainee type; others, more experienced, can be given appropriate responsibility in the working of the hospital or department, and might ultimately achieve the grade of "assistant" if the suggestions of the Platt Report[2] be implemented. A scheme of this type, originally designed by Mr. Linton Snaith, is now working very successfully at the Newcastle General Hospital.—I am, etc.,

Newcastle upon Tyne 2. HARVEY EVERS.

REFERENCES

[1] *Report of the Maternity Services Committee*, 1959. Ministry of Health, London.
[2] *Medical Staffing Structure in the Hospital Service. Report of the Joint Working Party*, 1961. H.M.S.O., London.

SIR,—As a general practitioner who is becoming a little despondent at practising obstetrics on soft, low beds in too well-furnished bedrooms, I welcomed the report of the Royal College of Obstetricians and Gynaecologists, cited by Sir John Peel (November 11, p. 1283), in its belief "that institutional confinement provides the maximum safety for mother and child, and therefore the ultimate aim should be to provide beds for all who need or will accept institutional confinement."[1] In short, domiciliary midwifery should follow the fate of kitchen-table surgery. It was adequate for its time, and now it is time to go.

I have just made a request via our local medical liaison committee to the Welsh Board of Health for consideration of a general-practitioner maternity unit of 18 beds in my area where a population of at least 50,000 people have no choice but consultant hospital beds round the periphery, which are always grossly overcrowded, or home, be it caravan or waterless farmhouse. Staffing of such a unit should be no problem, as I am sure the district midwives would be only too pleased to practise their profession under the conditions in which they were taught.

I understand that a consultant who pays a visit to a patient in a general-practitioner unit does not get paid a domiciliary consultation fee; this certainly should be rectified, as I agree fully with Mr. John Stallworthy's summing up of the recent meeting at the R.C.O.G. (November 11, p. 1283) that "teamwork and close

liaison, however, were essential between consultant and practitioner," and should not be discouraged.—I am, etc.,

Risca, Mon. P. M. VASEY.

REFERENCE

[1] *Report on the Obstetric Service under the National Health Service*, July, 1954 (revised 1956), p. 16, Royal College of Obstetricians and Gynaecologists, London.

SIR,—If the general practitioners in the Kingston Hospital area feel that the patients they themselves have selected as being likely to have normal pregnancies need consultant or senior registrar supervision at 36 weeks, or that any of their patients requiring, say, pudendal block should have it performed by a member of the anaesthetic staff of the hospital, then that is their own affair, but Mr. J. V. O'Sullivan's strong recommendation that general and maternity hospitals throughout the country should follow the scheme he describes (November 18, p. 1349) should, in my opinion, be strongly resisted.—I am, etc.,

Steyenton, Berks. A. SEMMENCE.

## The Contraceptive Pill

SIR,—We are writing in reply to the correspondence in the *British Medical Journal* of November 18 on the contraceptive pill.

In the first letter Dr. C. Edwards (p. 1354) asks how the Family Planning Association, in making "conovid" available in clinics, can pay due regard to the relationship with general practitioners. It has already been agreed by the Working Committee responsible for laying down the conditions under which oral contraceptives may be prescribed in F.P.A. clinics that "the doctor must be informed by letter and in no cases should pills be given to a patient who will not allow her G.P. to be notified." As it would be ideal to get the permission of the doctor beforehand, the routine letter to be used states that the patient is due to start the pill on (date) . . . and if the doctor does not get in touch before then it will be taken that he has no objections to his patient having the pill. We hope that Dr. Edwards and any other general practitioners who have any misgivings over this point will be reassured by these conditions. We can also reassure Dr. Edwards that, far from being harassed by the regular taking of the pills, the majority of the women are greatly relieved by the security they feel and are delighted with the simplicity of the method.

Dr. Arnold Klopper (p. 1354) shows concern over other aspects of the use of these oral contraceptives. He points out that the amount of oestrogen in the conovid tablet is in itself sufficient to inhibit ovulation in four cycles out of five, but for effective contraception by inhibition of ovulation a preparation must do this *every* time and this, in effect, is what the reliable progestogen–oestrogen mixtures, such as conovid, can do while oestrogen alone cannot. Dr. Klopper is misleading in stating that "there is no evidence that the antiovulatory action of nortestosterone compounds is due to anything other than oestrogen." Indeed, the evidence for their possessing much oestrogenic action—as judged, for example, from their effect on the endometrium, the vaginal epithelium, and the cervical mucus—is singularly lacking. Moreover, there is no question that progesterone itself can inhibit ovulation (it does so in pregnancy) and we have evidence that the progesterone derivative 17$\alpha$-acetoxyprogesterone cyclo-pentyl-enol-ether ("gestovis") can inhibit ovulation when given by mouth; this substance, at least, has no oestrogenic action. Dr. Klopper's feeling that oestrogen withdrawal bleeding is "excessive" can hardly be based on personal experience. The simple fact is that the progestogens alone do not provide adequate cycle control, whereas the addition of oestrogen facilitates this.

It is not true to state, as he has done, that in these trials endometrial biopsies were not done. It is true that they were not carried out in the Birmingham or Slough trials, but endometrial biopsies were carried out before medication, after one cycle and after several cycles of medication, in a good many patients in the London and Exeter trials. We would agree that a characteristic endometrial picture is found, but there is no evidence that this is in any way sinister—and it will be up to gynaecologists to familiarize themselves with this picture, especially as they will be using these progestogens more and more for control of abnormal menstruation. The considerable derangement of the menstrual cycle quoted by Dr. Klopper applies only to the patients on the Birmingham 1 OC trial (*Brit. med J.*, November 4, p. 1172), who were given what turned out to be an inadequate dose. The majority of women in the other trials, with adequate dosage, had regular menstrual cycles. Nor is it correct to talk about the large numbers of nauseated women—the figure for nausea that he quotes is only for the first month and in the majority of cases for a few days only.

So far as breakthrough bleeding is concerned, it must be remembered that these patients were under trial conditions and were being allowed to have breakthrough bleeding in order to determine the percentage of women who would continue to do so, and to find what proportion settled spontaneously. Of course, when oral contraceptives are used as an alternative method in F.P.A. clinics, if breakthrough bleeding does not quickly settle spontaneously measures will be taken to deal with this, if necessary by advising the patient to give up the method. However, from our studies with other preparations we are confident that oral contraceptives which produce far fewer side-effects, both subjectively and on the menstrual cycle, will soon be available.

When one remembers that oral contraceptive trials in various parts of the world have been going on for over six years, with no evidence of harmfulness emerging, it does seem, that Dr. Klopper's gloomy forebodings are a little out of touch with reality.—We are, etc.,

ELEANOR MEARS,
Medical Secretary, The Family Planning Association and Council for the Investigation of Fertility Control.
G. I. M. SWYER,
Chairman, Clinical Trials Committee, Council for the Investigation of Fertility Control.

London S W.1.

SIR,—I hope that when they hear about his attitude to the contraceptive pill Dr. C. Edwards's patients will rise up in revolt. Medicine is a service paid for by the public, which presumably has certain rights in this matter. Dr. Edwards's letter (November 18, p. 1354) is a classical example of the "holier than thou" attitude that is at present alienating the respect of the public for the medical profession. Modern man does not want his doctor to have this power of veto over him, nor is he prepared to accept *obiter dicta* from an Establishment which is often clearly reactionary.

Most progress is made in the face of Establishment opposition, and we are well known to be a reactionary

and protectionist profession. The Family Planning Association is a responsible, cautious, and well-advised organization, and it feels that the time is ripe to try the pill on a larger scale. Most patients have more common sense than they are usually credited with by their doctors. Surely it is the patient and not the doctor who decides which method of contraception is used. Sensible patients will ask (expert) advice on this subject —but if the doctor disagrees with the F.P.A., surely the final choice must be left to the patient. What, in fact, is a patient with a Catholic doctor supposed to do?

We ought as a profession to be very concerned about our public image. Dr. Edwards's attitude is reminiscent of those of our grandparents who demanded a man with a red flag to precede their motor-cars.—I am, etc.,

London W.9. H. BERIC WRIGHT.

## Progestogens and the Foetus

SIR,—We were interested to read your annotation on virilizing action of progestogens on the female foetus (November 4, p. 1205) and your comments that, from the studies reviewed, none of the oral progestogens tested was entirely free from virilizing effects on the female rat foetus. Those who fear the possible consequences to the foetus of progestational therapy in women during pregnancy were advised to abandon oral therapy.

Reerink *et al.*[1] have reported a new class of progestogens which do not depend only upon substituents in the steroid nucleus for their activity but also upon stereochemical changes at carbon atoms 9 and 10. These substances, named "retro-progesterones," have a 9$\beta$ hydrogen atom and a 10$\alpha$ methyl group as opposed to a 9$\alpha$, 10$\beta$ configuration of progesterone. Such stereo-isomeric analogues have interesting physiological activity. Tested in rabbits by the Clauberg method, the "retro-progesterones" show endometrial changes indistinguishable from those following the subcutaneous administration of progesterone.[2]

Schöler and de Wachter[3] have studied the effect of progestational compounds on the genital tract of rat foetuses when the compounds are administered during pregnancy. The substances which were given are available commercially and included progesterone, 6-dehydro-retro-progesterone ("duphaston"), 17$\alpha$-ethinyl-19-nortestosterone, 6$\alpha$-methyl-17$\alpha$-acetoxyprogesterone, 17$\alpha$-methyl-19-nortestosterone, 17$\alpha$-ethyl-19-nortestosterone, 3-deoxy-17$\alpha$-allyl-19-nortestosterone, 6$\alpha$,21-dimethyl-17$\alpha$-ethinyltestosterone, and 17$\alpha$-ethinyl-17-hydroxyestr-5(10)-en-3-one. These compounds were administered to female rats from the 15th to 21st day of pregnancy. All foetuses were sexed at birth by the method of Revesz *et al.*[4] and the sex so determined was confirmed subsequently by serial histological examination of the genital tract.

No newborn rats were found with the abnormal anogenital distance of 2–3 mm. (pseudohermaphrodites) in either of the groups treated with progesterone or 6-dehydro-retro-progesterone (duphaston). After giving these compounds, sex as determined by inspection of the internal sex gland was always in agreement with that determined by the anogenital distance. By measuring the anogenital distance in rats treated with the other synthetic compounds mentioned above, pseudo-hermaphrodites were detected in each case. Masculinization as evidenced by a penis-like clitoris, urethro-vaginal fistulae, or blind vagina—was also found in foetuses whose mother was treated with each of these synthetic progestogens but never in those given progesterone or 6-dehydro-retro-progesterone (duphaston). Therefore there is available an oral progestogen which, judged by the tests described, does not cause virilization in the female foetus.—I am, etc.,

NORMAN O. EVE,
Medical Department,
Crookes Laboratories Ltd.
London N.W.10.

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## Amputation Through the Knee

SIR,—I have read with interest the letter by Mr. Leon Gillis (November 18, p. 1355). Any contribution from the Ministry of Health Limb-fitting Service is always welcome, based as it is on a vast and unique experience. But I find it difficult to agree with all his conclusions.

First, let us not forget that it is not the stump but the patient who commands our first attention. Now an amputation for atherosclerosis is a major psychological event for the elderly, and the early healing of a useful stump is necessary if he is not going to lose heart and interest in the few remaining years of his life. Now, as I have recorded elsewhere, the blood supply of the skin flaps required for a Gritti–Stokes amputation is abundant, and I have an article shortly to be published showing this beyond doubt. Such blood supply is not enjoyed by the flaps required for amputation by disarticulation of the knee-joint. Healing by first intention after Gritti–Stokes amputation is to be expected, and indeed occurred in 76% of our recent patients whose age averaged 69 years, whereas after disarticulation such healing has in our small experience been unreliable. The blood supply of the flaps comes within the "dictates of pathology" to which Mr. Gillis refers as a guiding principle in amputation. Further early and sound healing allows a pylon to be fitted to a Gritti–Stokes stump within a month of operation, and even sometimes when healing is occasionally delayed.

Mr. Gillis suggests that sometimes a Gritti–Stokes stump might be considered end-bearing. It is not. All surgeons who practise this operation know that it is mostly ischial bearing and only lightly end-bearing, the latter to preserve proprioceptive sensation, an important advantage which he claims for the disarticulation stump only. He criticizes the long Gritti–Stokes stump because of the lack of space in the socket for any form of knee mechanism, yet he advises disarticulation where there is even less room. This part of his argument is difficult to understand and appears contradictory. Finally he emphasizes the difficulty in compensating for a hip flexion-deformity on the side of a Gritti–Stokes stump. I have never seen such deformity in this stump and the point in our experience does not arise.

I have been fortunate in my relationship with the limb-fitting services at Roehampton and at Cambridge, for both of which I have unbounded respect. Most excellent and functional prostheses have been supplied for my patients. Rigid and articulated pylons and permanent artificial limbs made on the same principle

have been supplied and have been most successful, though it must be admitted that only the fitter and more robust patients can control a free knee-joint. If my turn comes for amputation for atherosclerosis, I would like a Gritti–Stokes stump fitted with a Ministry of Health Limb-fitting Centre prosthesis.—I am, etc.,

London W.1. PETER MARTIN.

SIR,—I have difficulty in following the reasoning of Mr. Leon Gillis in his letter (November 18, p. 1355) extolling the virtues of a disarticulation of the knee in preference to a Stokes–Gritti amputation,

(1) The Stokes–Gritti amputation is at a higher level than a disarticulation, so his arguments proffered against the Stokes–Gritti must be more so in the case of the disarticulation. (2) Flexion deformity of the hip really should not occur with proper nursing and physiotherapy. (3) The blood supply to the skin and subcutaneous tissues is frequently very poor below the knee in the atherosclerotic subject, and the lower down the leg the worse it gets. The anterior flap of a disarticulation is too long and encroaches on this doubtful area, and in my experience the condyles of the femur are prone to slough through the flap.

I have performed the Stokes–Gritti amputation over 200 times in the past 15 years and I believe that it produces the best results of all in the elderly atherosclerotic subject when it is not practicable to perform a low amputation to allow him to walk.

While I would join Mr. Gillis in his praise of our Limb-fitting Service, there is still room for improvement, particularly in the time taken in delivery of pylons and limbs after the first fitting. One of the most important aspects of the treatment of the elderly amputee is early ambulation, and this is unduly delayed in many instances waiting for the prosthesis.—I am, etc.,

Essex County Hospital, Colchester. ROLAND N. JONES.

## Nuclear War

SIR,—The lives of young people are overshadowed by the possibility of nuclear war. I know from my own children and their friends that this is so.

I was a combatant in 1914, and put on uniform in a spirit of romantic adventure. War was never noble, but illusions of its nobility were then finally destroyed. The passing years showed how the hatreds and frustrations left by world war I led to the threat of world war II, and how difficult it was for governments to give up national interests for the sake of international co-operation. Finally war became impossible to avoid, in spite of the desperate last-minute efforts of statesmen. In these wars negotiated peace was possible, but rejected. In the first world war soldiers of all the armies were in a state of actual or threatened mutiny before peace was made. The second war was marked by the attempt to force submission through terror, and by the deaths of millions of civilians as well as equally "innocent" conscripts, and, before its end, the total destruction of Hiroshima and Nagasaki each by a single explosion.

The cause of war is no more simple or single than the cause of disease. To think of war as disease, as more than one of your contributors has advised, is not illogical, but rational, unless one is able to regard war as stimulating, fruitful, and inevitable, rather than degrading and destructive. There are some quite clever people who say that they do so regard it; these are not influential, but there are very many more who have not really acknowledged to themselves that everything about war is evil, and that so long as war remains a possibility we permit ourselves to think of it as having some quality of nobility.

The pathogenesis of disease is the proper study of our profession. The first national conference on the pathogenesis of war was held at Cambridge this year, and the second is planned for Oxford in 1962. But understanding of causation need not come before attempts at prevention. To create conditions in which nuclear war, which we all now realize means world suicide, cannot occur requires that more and more people express their indignation that it is still possible for governments to prepare for war. It would not be true to say that any government actually uses the threat of nuclear war to further political ends, but neither has the government of any one major nation except India made any clear statement that nuclear war is absolutely ruled out as an instrument of policy.

I do not myself believe that if either the U.S.S.R. or the U.S.A. abandoned nuclear arms any material advantage would follow for the "other side." Political ends are not now to be realized by mass destruction or the threat of it. But unilateral nuclear disarmament by either government would require such a revolutionary change of attitude as to be inconceivable. Agreement to disarm, however, is certainly a practical aim, and is the only way of preventing nuclear war from following some sudden increase of tension and a display of "firmness" in which a reckless decision to explode a nuclear weapon could be made by some excited individual or even by accident. For disarmament to be possible there must be political compromise, and governments must know that they are acting with popular support. The "Pugwash" conferences between scientists of "East" and West have already helped to create this.

The medical profession has a good reputation for social responsibility. Its essential purpose is to make life better, not to destroy it, and it has, more firmly established than any other profession, international obligations and associations. I hope that the medical profession in England will take the initiative in obtaining the help of doctors in all countries to support their governments in abandoning the threat of war in furtherance of what each of them regards as their legitimate aims.—I am, etc.,

Bickley, Kent. DUNCAN LEYS.

SIR,—Recent correspondence in your columns suggests to me that some members of our profession indulge in very muddled thinking. One has only to read the official history of world war II dealing with the home front to realize fully what a life-saving organization Civil Defence proved itself to be. Just before the war the confidential official estimate of the fatal casualties to be expected in a month's blitz was some 600,000. In the event the total for the six years of the war was about 60,000. For many years in the Royal Navy and in Civil Defence I have been involved in detailed study of the medical problems of all forms of warfare—conventional weapons (i.e., high-explosive and incendiaries), chemical (gas) warfare, biological (germ) warfare, as well as nuclear weapons. While wholeheartedly at one with my pacifist colleagues in abhorring any form of warfare, I hope that I, and others like me, will continue

to study how to mitigate its horrors and to play an informed role in life-saving instead of sitting down and crying, "Woe, woe!"—I am, etc.,

Havant, Hants. J. G. HOLMES.

SIR,—I would like to know if other doctors besides myself have had requests made to them for a lethal dose of some drug in case of nuclear war. During the past few months several people have asked for just this—for themselves, their children, or their grandchildren. The requests were not made in fear of personal suffering, but with the emphasis on the family as a unit. A dying mother would not wish to leave a young child or an aged parent alive yet helpless, and possibly also doomed to die shortly from radiation sickness or burns or injuries; a husband might wish to put his wife out of her agony.

Perhaps these people are not more selfish but more realistic than most. Certainly the requests did not seem unreasonable to me, and far more practical than most present Civil Defence measures. But all the same I revolt at a situation that calls for handing out cod-liver oil to babies with one hand and lethal drugs with the other. Whatever made me become a doctor now makes me refuse to condone the wholesale destruction of my fellow creatures by modern weapons of war. I could not wish to drop an atomic bomb on anyone, even if one was dropped on this country first.—I am, etc.,

London N.W.3. PHYLLIS M. DOBBS.

SIR,—In associating myself with other medical practitioners against the manufacture and possible use of nuclear weapons, I have asked myself what can we doctors do apart from protesting. This is the answer:

Unless we support the apparently official U.S. policy that 50 million British people and 70 million Americans can be dispensed with following a surprise attack with nuclear rockets by Russia, which could herself be annihilated afterwards by the remaining stock of U.S. nuclear weapons, we must admit that for Great Britain a policy of nuclear armaments is equivalent to suicide, and that therefore we must destroy all nuclear arms, even the smallest ones, in our possession.

Secondly, we must refuse to participate in Civil Defence in any form whatsoever, even attending lectures. C.D. in a nuclear war gives the illusion that something can be done to prevent or diminish the effects of nuclear bombing, and that, by sacrificing the majority, the minority can be saved, a policy contrary to the most elementary ethical feelings of both religious people and atheists.

Thirdly, we must avoid seeing everything in black and white by equating Russia with the powers of darkness—like Dr. Robert Cutler does (November 4, p. 1225)—and the West with the powers of light. Surely there is also a lot of good in Russia and a lot of bad in the West, especially in the U.S.A., just as there is in any other country. The suppression of liberty in Russia (a liberty, by the way, which the Russians have never known) is just as bad in its kind as the exploitation of the masses by high-pressure salesmanship of an irresponsible kind in the West.

I wonder why medical experts in mass psychology have not expressed any opinion on this matter (does not the Charter of U.N.O. say that "War originates in the minds of people"?), and why statesmen do not ask for their advice how to cure the war hysteria and anxiety neurosis which exist on both sides of the iron curtain.

Finally, a world conference either of the World Medical Association or of W.H.O. with Unesco should be convened with the participation of doctors from East and West to discuss ways and means of persuading their governments to suspend further nuclear tests in any form and to start a programme of psychological disarmament, including cessation of hostile radio, T.V., and press propaganda, reform of history teaching, and increasing exchange of postgraduate students and others.—I am, etc.,

Nottingham. G. FIELDING.

*** This correspondence is now closed.—ED., *B.M.J.*

## Chronic Sick of Psychiatry

SIR,—The letters from Dr. J. A. R. Bickford (November 18, p. 1358) and Dr. Geoffrey Tooth (p. 1359) present the depressing spectacle of two important people in British psychiatry writing largely at cross purposes. Like Dr. Bickford I have great difficulty in visualizing a chronically ill patient who requires "no more than custodial care" (Dr. Tooth's phrase). Dr. Tooth in his letter, attempting to justify the phrase quoted, refers to a category of patients in whom a need for hospital care depends as much on social as medical considerations, and then goes on to suggest that specific provision should be made in future planning for those patients "who need custodial care in a hospital setting . . . ," which "does not, of course, exclude treatment." I think if this correspondence is to serve any useful purpose whatsoever Dr. Tooth should state very precisely in what clinical category or categories these patients fall. I wonder how much they have in common with the patients with whom Dr. Bickford and all psychiatrists working in mental hospitals are largely concerned, and what is the size of the problem they present.

Surely one of the major lessons which British psychiatrists have re-learned in the last 30 years is that many patients who were thought to require "no more than custodial care" did not require custody at all but required treatment which they are now starting to get and which has produced the striking fall in mental hospital populations with which the Minister is quite justly gratified. It will be a great pity if a return to the concept of third-class patients and fourth-class treatment reverses this trend.—I am, etc.,

Shenley Hospital, Nr. St. Albans, Herts. D. T. BARDON.

## Peptic Oesophagitis

SIR,—I write in support of Mr. H. Daintree Johnson's comments (November 18, p. 1361). In general it is too readily assumed, in patients with sliding hiatus hernia and oesophagitis, that the hernia is the cause of the oesophagitis.

It is unfortunate that there is as yet no method of studying the function of the longitudinal muscle coat of the oesophagus. The standard barium-swallow examination of the oesophagus, either by the usual radioscopy or by cinefluoroscopy, shows the function of the circular muscle, particularly at the upper and lower ends. But in the normal oesophagus the circular muscle forms a very small proportion of the muscular structure, and one cannot study movement of the longitudinal muscle by inference from the movement of a radio-

opaque bolus within the oesophagus. Similarly pressure measurements taken from the oesophageal lumen at rest and during swallowing reflect only the activity of the circular muscle. It seems to me that there will be no true understanding of abnormal regurgitation at the cardia, sliding hiatus hernia, and oesophagitis until a method of study of the longitudinal muscle-coat function has been devised.

It is unlikely that all cases of sliding hiatus hernia have a common cause. In some the hernia may arise as a result of increased intra-abdominal pressure associated with laxity of the hiatal muscle and fascia of the diaphragm; but in others it is likely that disorder of the function of the oesophagus and possibly of the stomach—in fact of the fore gut—is responsible for abnormal regurgitation, with oesophagitis, with hernia, or with both. It is in these cases that recurrence after operation is most likely, since nothing is done at operation to influence the underlying disorder of function.—I am, etc.,

Cardiac and Thoracic Unit,
Southampton Chest Hospital,
Southampton.

K. S. MULLARD.

## Experiments on Animals

SIR,—Most medical men are neither anti-vivisectionist nor lovers of rats: but one need be neither to be distressed at the detailed sufferings of these animals recorded in the article on p. 1194 of the *B.M.J.* of November 4. In this experiment it is stated that stiffness, swelling, and whitish discoloration of the skin of the snout developed. "These lesions progressed rapidly, and towards the end of the experiment the rats could no longer close their mouths . . . developed a gasping type of breathing . . . had obvious difficulties in their attempts to swallow the occasional crumbs of food they were able to ingest. . . ."

Had this research revealed some new facts that would have been of value clinically there would be at least that to weigh against this inhumane treatment; but in the penultimate paragraph it is admitted that it has little relevance to human pathology. I feel sure that people of balanced opinions, both medical and lay, will be strongly opposed to this treatment of defenceless animals even if they are classed as vermin. Academic knowledge can be bought at too high a price, and one has to admit that the anti-vivisectionists may not be overstating their case after all.—I am, etc.,

St. Leonards-on-Sea,
Sussex

W. GOVER.

## Neuropathy after Thalidomide ("Distaval")

SIR,—We were interested to read that Drs. B. W. Meade and S. B. Rosalki (November 4, p. 1223) have demonstrated impairment of glucose absorption in a patient with thalidomide neuropathy. We have reviewed the details of similar investigations on our patients. Glucose-tolerance tests were performed on six patients while they were still taking thalidomide regularly each night. Five of these showed a normal rise of blood glucose after 50 g. of oral glucose. The rise from the fasting level varied between 43 and 113 mg.%. Only one patient had a "flat" glucose-tolerance curve, with a rise of 17 mg.% after 30 minutes. Another case has been investigated in more detail recently. A glucose-tolerance test three weeks after stopping thalidomide showed a normal rise of 56 mg.% from the fasting level. She then took 300 mg. a night (her usual dose) for a week and glucose-tolerance tests were repeated on the third and seventh days. The rise of blood sugar was similar on each occasion (50 and 60 mg.%). Of these seven patients only one showed any evidence of impaired glucose-absorption.

In five patients simultaneous urine examination was carried out and three showed 0.5% sugar in the urine at blood-glucose levels of 140, 153, and 163 mg.% respectively. Since these blood levels are below the accepted normal renal threshold it seems possible that tubular reabsorption of glucose might be impaired. Further studies along these lines are being carried out.

In the five months before our paper was published (September 30, p. 855) we saw a further eleven patients with thalidomide neuropathy, the clinical features being identical with those of the reported cases. Since publication there has been a relative increase in the number of cases seen.

Drs. T. N. Rudd and R. N. Greenhalgh (November 11, p. 1287) suggest that small doses of the drug may be less harmful than larger ones. This, however, is not our experience. In particular we would like to mention a colleague who developed cramps in the legs and numbness of the feet after taking only 25 or 50 mg. thalidomide two or three times a week for a year. We have now seen a brother and sister who developed identical symptoms at the same time interval after starting thalidomide. These two observations support our tentative suggestion that development of symptoms depends on individual susceptibility to the drug and may bear no close relation to the total amount of thalidomide taken.—We are, etc.,

Department for Nervous Diseases,
The Middlesex Hospital,
London W.1.

MICHAEL KREMER.
PAMELA M. FULLERTON.

SIR,—I have followed the correspondence concerning thalidomide with special interest because I am one of the unfortunates who developed a peripheral neuropathy. There was a time when I and some of my partners thought we had found almost the ideal sedative in "distaval." My neuropathy was spotted thanks to the excellent piece of observation and deduction by Dr. A. Leslie Florence, to whom I will always be most grateful for his letter (December 31, 1960, p. 1954). Until then I felt I must be getting neurotic and imagining symptoms, never dreaming of associating them with the drug which we were frequently prescribing.

It is now over ten months since I stopped taking distaval and my symptoms are no better. I find the condition more trying over a period of time than other departures from health of a more serious nature which have been my lot of recent years. An incidence of 1 in 250 may seem trivial, but not if you are one of those involved and with but little evidence that the condition is reversible.—I am, etc.,

Maldon, Essex.

IVAN PIRRIE.

SIR,—In relation to an advertisement appearing in the *British Medical Journal*, Dr. J. Tewson (November 18, p. 1360) asks, "Whom can we believe?" Surely the answer is, we can believe in ourselves—in our own clinical observations, assisted by our own evaluation of the claims made by others, no matter from what source they may come. I am sure that Dr. Tewson would be

among the first to fight any suggestion that medical literature should be censored. Why, then, should he demand (and, from the Editor's footnote, evidently receive) censorship of advertising literature to the profession?

That the advertisement in question, "This child's life may depend on the safety of 'Distaval,'" is not far from the truth I have seen for myself, as no doubt others have too. Nine months ago I saw a 16-month-old child who had swallowed twelve 100-mg. tablets of distaval, which he had taken from his mother's handbag. He slept soundly for about 16 hours, but could be roused to take his food. He made an uneventful recovery. The outcome, however, would have been much more serious if the tablets had been, say, one of the barbituric acid derivatives.—I am, etc.,

Liverpool 14. E. F. SWIFT.

### Withdrawal of Thalidomide ("Distaval")

SIR,—Since sending you my letter concerning peripheral neuritis (November 25, p. 1435) reports have been received from two overseas sources possibly associating thalidomide ("distaval") with harmful effects on the foetus in early pregnancy. Although the evidence on which these reports are based is circumstantial and there have been no reports arising in Great Britain, either clinically or pharmacologically, we feel that we have no alternative but to withdraw the drug from the market immediately pending further investigation. We are also withdrawing "valgis," "valgraine," "asmaval," and "tensival," all of which contain thalidomide.

We will continue to carry out pharmacological and other studies of our own, and you may rest assured that the medical profession will be kept fully informed of developments.—I am, etc.,

D. J. HAYMAN,
London S.W.19. Managing Director,
The Distillers Company (Biochemicals) Ltd.

### Non-barbiturate Hypnotics

SIR,—In the leading article (September 30, p. 876) that followed the paper by Drs. Pamela M. Fullerton and Michael Kremer (p. 855) on thalidomide neuropathy it is stated that the perfect hypnotic has not yet been discovered. This is not contested, but the same leading article also says that further research is needed to find additional, safe, non-barbiturate hypnotics which do not have the disturbing side-effect of neuropathy. I cannot claim to be an expert in nocturnal hypnotics, but an extensive experience of these drugs in general practice makes me doubt whether such research is as essential as suggested.

It is, of course, true that patients vary considerably in their response to sedative drugs, so that no single drug in one dosage form is likely to suit all patients. Nevertheless, careful use of some of the available non-barbiturate hypnotics can satisfy the needs of the vast majority of patients.

As mentioned by Drs. Fullerton and Kremer, glutethimide ("doriden") does not have similar neurotoxicity and is an extremely useful drug which gives very good results in many patients, although it is sometimes not potent enough and higher doses produce morning hangovers. Another compound coming in much the same category is dichloralphenazone ("welldorm"), which is safe but lacking in potency for resistant patients. A more recent introduction is propiomazine ("indorm"), which is apparently as safe as the closely related promethazine and which I have found very useful and effective in most patients. It appears to be suitable for neurotics, for adolescents, and for the elderly. It was not very helpful in depressed subjects nor in those whose insomnia was due to pain, unless an analgesic was combined with the sedative, in which case potentiation between the two drugs was noted.

None of the non-barbiturate hypnotics described above will be the optimum preparation for all patients, but it seemed to be worth while mentioning that a problem can often be solved by the discriminate use of existing drugs instead of always running to make a frantic search for new ones.—I am, etc.,

London N.W.6. L. REDHOUSE.

### Wooing Sleep

SIR,—From time to time, even though completely comfortable, I find myself unable to sleep owing to unintentional cerebral activity. I sometimes have then tried to emulate a principle of Yoga, and by an effort of will I have succeeded in concentrating on "nothing" for long enough to pass into a state of somnolence. More often I have failed to keep my mind blank for longer than several seconds at a time and have ended up by reading, or something similar, for the next hour or two.

Recently I have tried an aid to the exclusion of "extraneous" thoughts also practised in Yoga—namely, a focusing of the consciousness on respiration. I concentrate on breathing in a rhythm which I imagine is similar to that which I use in sleep. I find I can focus my attention on the act of breathing and hold it there more easily and for a longer time than I can concentrate on "nothing" or "counting sheep." In both the latter examples extraneous thoughts repeatedly intrude. As my concentration on respiration gradually tires, voluntary control seems to lapse naturally into involuntary control, and no new line of thought seems to replace the focus of attention which is gradually relinquished. On the last two or three occasions that I have concentrated on respiration, I have fallen asleep within 5 or 10 minutes.

Training may be necessary to sustain uninterrupted concentration long enough to damp down unwanted cerebral activity. I should therefore not expect this method to provide a panacea for sleep induction, though I would be interested to know whether others who try it are rewarded with success.—I am, etc.,

Brighton, Sussex. J. E. JAMESON.

### Early Weaning and Ulcerative Colitis

SIR,—The interesting hypothesis of Drs. E. D. Acheson and S. C. Truelove (October 7, p. 929) that early artificial feeding increases the liability to ulcerative colitis might gain support from our observations. Ulcerative colitis is excessively rare among the Zulu population whom this hospital serves. During the past three years some 47,000 patients have been admitted to the general wards. Among these there has been one who might have ulcerative colitis in an early stage, though the clinical and radiological features of this case are still indefinite. The diagnosis has not been considered in any other case.

In this predominantly rural and unsophisticated community breast-feeding is the rule. Weaning before the age of 14 days is very unusual. When it does occur the infant's chances of survival are small, since artificial feeding in these circumstances presents numerous difficulties and hazards.—I am, etc.,

Edendale Hospital,
Pietermaritzburg, Natal. J. E. COSNETT.

## Trends in Child Psychiatry

SIR,—The Association of Undergraduate Teachers of Psychiatry, which counts amongst its members representatives of nearly all the undergraduate teaching schools in Great Britain and Northern Ireland, has recently considered a memorandum drawn up by a subcommittee with the above title. At a recent meeting of the association we were instructed to submit this memorandum to you with a view to its publication.

(1) The responsibility for providing child psychiatric services is divided at present between the Ministry of Health on the one hand and the Ministry of Education acting through the local education authorities on the other. There are approximately 100 child psychiatric clinics which are solely the responsibility of the Ministry of Health. These are in general hospitals for the most part, and the majority of teaching hospitals provide such clinics. There are approximately 120 child psychiatric clinics which are the *joint* responsibility of the Ministries of Health and Education, and there are about 130 such clinics provided by the education authorities alone. There are thus more clinics for which the Ministry of Education takes responsibility (250), either jointly with the Ministry of Health or alone, than those for which the Ministry of Health is responsible (100). The staffing structure and the orientation in these two groups of clinics is, in general, somewhat different. The "education" clinics are generally headed by educational psychologists who are full-time employees and may operate in a number of clinics in their areas. The psychiatrist in the team may be employed by the education department or may be seconded by the National Health Service for the work, usually on a sessional basis.

(2) We consider that the term "guidance" is unfortunate in that, like marriage guidance and vocational guidance, it suggests an activity which can properly be carried out or supervised by those who are not medically qualified. We believe indeed that only a misunderstanding about the meaning of the word could explain the Ministry of Education's statement that "Child guidance in the broadest sense is synonymous with education itself. . . ."[1] Most of us have been in charge of psychiatric clinics for children over a period of many years, and it has been our experience that most patients attending them have shown pathological anxiety with or without symptomatic behaviour disorder, physical symptoms, psychosomatic disorders, or psychoses; or have been below average intelligence. We have not seen many instances where "guidance" in any way covered the work that was done.

(3) While it is generally true that drugs and physical treatments have a smaller place in the treatment of emotionally disturbed children than in adults, we believe that a knowledge of medical psychology, general psychiatry, and internal medicine is essential in those bearing the responsibility for diagnosis and the direction of treatment. For these reasons an educational psychologist and a paediatrician without psychiatric training seem quite unsuitable as directors of psychiatric clinics. Yet both of these things occur whether or not the director is so described. At the same time we would not wish to seem to underestimate the vital roles played by psychologists and psychiatric social workers employed in a psychiatric framework.

(4) We feel that a paediatric hospital or the paediatric department of a general or teaching hospital is always the ideal site for a psychiatric clinic, offering as they do the advice of colleagues and the usual hospital services.

(5) We regret the dominant role of such bodies as the Care Committees of London which are under the control of the local education authority. This tends to exclude the general practitioner from the scene, to exclude doctors of the local health authority, and to destroy the confidence that parents should have that their affairs are secrets between them and the doctor.

*Recommendations*

(1) The term "child guidance" should be abandoned and the alternative "child psychiatry" should be used in all cases.

(2) The director of a child psychiatric clinic should in all cases be a consultant psychiatrist with experience of adult work.

(3) A paediatric hospital or department is the ideal site for a child psychiatric clinic and the out-patient department should be supported by beds under the control of the psychiatrist.

(4) We are firmly convinced that at national level child psychiatry should be the responsibility of the Ministry of Health.

(5) We do not believe that child psychiatry is a legitimate preoccupation of the education authorities.
—We are, etc.,

DESMOND CURRAN,
Chairman,
GERALD GARMANY,
Honorary Secretary,
Association of Teachers of Psychiatry
in Undergraduate Medical Schools.

REFERENCE
[1] Ministry of Education Circular 347, March 10, 1959.

## Chloramphenicol and Aplastic Anaemia

SIR,—Although in the early days of its use chloramphenicol was shown to be marrow toxic, more recently Ioannidis and Murdoch[1] concluded that it had a place in the treatment of bronchitis and that in a dosage of 10 g. the toxicity was negligible. Dameshek,[2] however, considered that chloramphenicol was a factor in eight of his series of 30 cases of aplastic anaemia. As there appears to be no case recorded in British literature of aplastic anaemia due to chloramphenicol in a dosage of under 10 g., we feel we should draw attention to a case seen in this hospital.

A boy aged 10 years who had asthma with frequent associated attacks of bronchitis was given chloramphenicol in a total dosage of 2.5 g. over a period of five days for an exacerbation of his bronchitis. Four weeks after the course of chloramphenicol he showed spontaneous bruising. He was seen by us for the first time two weeks later, at which stage his haemoglobin level was 8.1 g./100 ml., the white cell count 1,500, 94% of the cells being lymphocytes, and thrombocytes were absent. Sternal puncture showed no evidence of active marrow. The child's condition did not improve despite attempted

treatment and the child died five weeks after his admission. Post-mortem examination showed no evidence of functioning marrow.

Although aplastic anaemia can arise spontaneously, it was felt that chloramphenicol was the causal agent in this case.—We are, etc.,

Highlands General Hospital, London N.21. G. MELTON. P. BEAGLEHOLE.

REFERENCES

[1] Ioannidis, A. H., and Murdoch, J. McC., *Brit. med. J.*, 1957, **1**, 1157.
[2] Dameshek, W., *J. Amer. med. Ass.*, 1960, **174**, 1853.

## Why Drink Milk?

SIR,—I think it is agreed by all that in the vast majority of cases mother's milk is the natural and adequate food for the infant mammal. But the articles by Drs. K. B. Taylor and S. C. Truelove (October 7, p. 924) and Drs. E. D. Acheson and S. C. Truelove (p. 929), and the letter from Dr. B. McNicholl (November 4, p. 1219) confirm my belief that after the age of weaning further consumption of milk (especially a "foreign" one—e.g., cow's milk) is neither natural nor necessary—and there are other and many milk-borne diseases besides ulcerative colitis.

Is it not time the British Medical Association should state unequivocally whether or not milk is a desirable article of diet? There is no particular virtue or value in milk that cannot be replaced by "safer" foods. Again I ask, why drink milk?—Baby Food!—I am, etc.,

Dundee. F. R. BROWN.

## Bathing in a Plaster

SIR,—I have found recently great benefit from the use of polythene plastic bags placed over a limb encased in plaster-of-Paris or adhesive strapping when a patient wishes to take a bath. It is, generally speaking, very difficult to have a bath with a below-knee plaster propped on the edge, and the result of such efforts is almost always some degree of wetting and softening of the cast. If, however, a polythene bag is put over the limb and secured with a couple of elastic bands, the patient can bath with relative safety. Often, being able to have a bath is the one item that determines whether a patient will accept a plaster cast.—I am, etc.,

Winchcombe, Glos. JOHN FINCH.

## Hypertension of Pregnancy

SIR,—In the annotation on hypertension of pregnancy (October 14, p. 1007) you discussed hysterotonin as an aetiological factor in its production. Your evaluation, however, failed to include many pertinent criticisms to which I wish to draw attention. When substances are seriously considered as responsible for sustained hypertension certain criteria must essentially be satisfied, since there are over a score of polypeptides with hypertensive properties that have been rejected as agents in the production of hyperpiesia in the human. Importantly, they need identification by their chemical structure; then their amounts in circulation must be considered sufficient to maintain a raised blood-pressure; and again specific substances need to be found that antagonize their hypertensive effects; whilst finally intra-arterial (*not* intravenous) injection must be employed in demonstrating their activity.

None of these criteria have been satisfied. The authors claiming this specificity[1 2] had failed to recognize that both renin and vaso-excitor motor substance have already been found to be present in pre-eclampsia. The properties of the octapeptide of angiotensin II entirely correspond to those enumerated as peculiar to hysterotonin, for not only does it elevate the blood-pressure but it produces uterine contractions and is not destroyed by adrenolytic agents. The sole point of difference—quite reasonably accounted for by the impurity of hysterotonin—is the fact that the angiotensin is dialysable whereas the hysterotonin is not.

In their claim for the aetiological significance of hysterotonin they set out the underlying influence of an increased uterine tension, which, by effecting myometrial ischaemia, causes an insufficient oxygenation of the decidua that is responsible for the product. It is already well recognized that the utero-renal reflex depends on the resistance of the uterus to stretch for its foundation—a common ground thereby shared. That the placenta or decidua cannot have a primary role in the production of pre-eclampsia is entirely borne out by the fact that pre-eclampsia is recovered from on the death of the retained foetus only to recur days later at the onset of labour. Reflection will show that such a happening denies any relevance of the primary intrusion of placenta or decidua in the toxaemic aetiology, but underlines the undeniable significance of the utero-renal reflex that in all the circumstances can alone explain this recurrence.—I am, etc.,

Worthing, Sussex. J. SOPHIAN.

REFERENCES

[1] Hunter, C. A., and Howard, W. F., *Amer. J. Obstet. Gynec.*, 1960, **79**, 838.
[2] —— ibid., 1961, **81**, 441.

## A Case for Diagnosis

SIR,—The diagnosis of porocephalosis proposed for the case presented (September 23, p. 820) cannot be rejected so easily (October 14, p. 1027). (1) The patient didn't eat any snake during his trip to Africa. The eggs of *Armillifer armillatus* can be absorbed with snakes, but also with water soiled by snakes. So this infestation is very common in Africa: Vaucel[1] states that 5–25% of Africans in certain regions have porocephalosis. (2) The typical horseshoe calcifications, well described by Drs. Zaida M. Hall and R. R. Wilson (September 23, p. 280), appear many years after infestation, as Pellegrino[2] stated in a recent paper. The period of ten years between an African trip and appearance of calcifications is not unusual.[3 4] (3) The biopsies photographed by Drs. Hall and Wilson in the paper showed only connective tissue changes, and no calcification. Therefore it seems reasonable to think that the radiological, horseshoe-like object was missed by the biopsies.—I am, etc.,

Swiss Tropical Institute, Basle. MICHEL FERNEX.

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[1] Vaucel, M., *Médecine Tropicale*, 1955. Flammarion, Paris.
[2] Pellegrino, A., and Cave, L., *Méd. Afr. noire*, No. Spécial, August, 1960, p. 128.
[3] Woithelet, G., *Méd. trop.*, 1956, **16**, 379.
[4] Van Wymeersch, H., and Wanson, M., *J. Radiol. Électrol.*, 1955, **36**, 22.

## "A Case of Renal Failure"

SIR,—The Clinicopathological Conference (November 4, p. 1208) was most interesting indeed. The most puzzling aspect of the case was a very rapid deterioration with failure of response to several attempts at dialysis. Renal-vein thrombosis was mainly blamed for this dramatic downhill course.

After looking at the necropsy report no comment was made on the amyloidosis of both adrenals of this patient. I wonder if this had any part to play in his final illness? If he had latent adrenal insufficiency, the stress of his condition could certainly have worsened it. This would fit in with his extreme electrolyte disturbances and the failure of response to dialysis. True that this patient's blood-pressure on admission was normal, but then in view of his renal condition the experts were expecting a high blood-pressure. Also his blood-pressure levels before the onset of the final illness were not recorded and the enlargement of the heart was left unexplained. Could it be that this patient had had previous high blood-pressure causing some cardiac enlargement and his so-called normal blood-pressure in his final illness was a relative state of hypotension for him, reflecting the failure of adrenals?

I shall be grateful to know what Dr. Milne says about adrenal amyloidosis as a cause of adrenal failure in general and in particular reference to this patient.—I am, etc.,

Edinburgh. S. AHMED.

### Free Beer

SIR,—I find your correspondent's reaction (November 11, p. 1293) to the offer surprising and fail to see why a letter of commendation should be held to lower the prestige of the profession. The implication in his letter that for the sake of 12 bottles of beer we are likely to have so little integrity as to recommend it to our patients if we do not believe in it is a far deeper insult to the profession.

A tonic after an illness is an accepted form of therapy. What could be more suitable than a substance which stimulates the appetite, induces a feeling of well-being, and is followed by a mild sedative action which allows the patient to doze pleasantly for an hour after lunch? More able pens than mine will doubtless evaluate alcohol as a therapeutic agent, but it would seem to me to be preferable as a tonic to a mixture of synthetic vitamins fortified with dextro-amphetamine sulphate.

Dr. A. Spencer Paterson's views would have perhaps commanded more respect had he not commenced his letter with a sneer in not very elevated taste.—I am, etc.,

Corbridge, Northumberland. GEORGE S. JEANS.

### Routine Immunization

SIR,—The criticism of Dr. A. Hollman (November 11, p. 1292) is perfectly correct. The needle I use for injection of babies is called No. 17, but is actually 25 Standard Wire Gauge. The particular needle, a quarter of an inch (6.4 mm.) long, is made by Messrs. Reynolds and Branson, of 13 Lower Briggate, Leeds. I mention this because I have had a number of inquiries for this type of needle.—I am, etc.,

Rothwell Haigh, Nr. Leeds, Yorkshire. C. E. GOLDSBOROUGH.

### Presentation of Glyceryl Trinitrate

SIR,—May I add my plea to that of Dr. Mackenzie (November 4, p. 1227) for a return of the chocolate tab. trinitrini—especially the thin flat ones? Many patients say they much prefer them. Why? "The white ones give me a headache." "The old brown ones seem to work better." "The old ones are a handier shape." "The flat ones are easier to divide."—I am, etc.,

Stevenston. F. ROSS.

# Obituary

## T. H. G. SHORE, M.D., F.R.C.P.

Dr. T. H. Gostwyck Shore, emeritus physician to the South Devon and East Cornwall Hospital, died in Bournemouth on November 17. He was 74 years of age.

Thomas Henry Gostwyck Shore was born on June 21, 1887, the son of Dr. Thomas W. Shore, who was for many years dean of the medical school at St. Bartholomew's Hospital. After distinguishing himself as a student at Cambridge, where he gained first-class honours in both parts of the Natural Sciences Tripos, he went on to St. Bartholomew's Hospital, qualifying in 1911 and graduating M.B., B.Ch. in 1913, the year in which he won the Lawrence research scholarship. In 1914 he took the M.R.C.P. After holding the posts of casualty physician and house-physician he was appointed demonstrator in pathology at Bart's and, later, curator of the museum. On his return from service in the R.A.M.C. during the first world war he proceeded M.D. and went into practice as a consulting physician in London after his election to the honorary staff of the Metropolitan Hospital. He became F.R.C.P. in 1927.

In 1930 he was appointed senior honorary physician to the Prince of Wales Hospital (now the South Devon and East Cornwall Hospital), Plymouth, a position he held until his retirement in 1952. In addition to his work as a busy and popular consultant, Dr. Shore took an active part in the affairs of the B.M.A. During his last year in London he was chairman of the City Division and in 1948–9 chairman of the Plymouth Division. At the Annual Meeting in Plymouth in 1938 he was president of the Section of Medicine. In addition he served on a number of central committees, including the Central Medical War Committee and, for one year, the Central Consultants and Specialists Committee. For many years he was chairman of the medical board in Plymouth as well as of the local medical war committee, and he was also a justice of the peace for the city.

C. C. P. writes: During an air raid on Plymouth Dr. Shore's beautiful home in the Crescent sustained a direct hit from a high-explosive shell and he lost nearly all his possessions. He re-established himself in a house in Mannamead, and this too was completely destroyed by incendiaries. In spite of all his misfortunes he showed amazing courage in carrying on his heavy responsibilities in caring for the many patients in Plymouth and in South Devon and Cornwall, where his services as a consultant were in constant demand. An able diagnostician, he had the power of instilling confidence and reassurance to the sick. He was immensely popular with all his colleagues, for he was always cheerful, with a fund of stories and reminiscences. He is survived by his widow and an only daughter.

S. N. S. writes: "T.H.G.," as he was known, was a man of quiet and unassuming manner whose human approach to medicine was one of his most valuable assets. He was a great believer in the old adage, "Treat the patient and not the disease," and patients always felt better after seeing him—this I can testify from my personal experience. He was well read and versed in English literature, and one of his characteristics was that he always managed to bring in some well-known quotation to illustrate his point: if there was no apposite quotation from the classics he was not at a loss, for he could always find an alternative from Gilbert and Sullivan—this, delivered with an infectious chuckle, helped to put patients at their ease. An active member of the B.M.A., he was for many years a member of the executive council of both the South-western Branch and the Plymouth Division, and was chairman of the Plymouth

Division in 1948. In order to encourage the younger members of the profession to take more interest in the B.M.A. he was largely instrumental in inaugurating "supper" meetings, and these proved sufficiently attractive to increase the attendance considerably. His ethical standards were extremely high and his advice on personal and non-medical problems was frequently sought and willingly given. He was, in truth, an "elder statesman."

## ERIC WORDLEY, *M.C.*, M.D., F.R.C.P.

The sudden death of Dr. Eric Wordley at his home in St. Mawes on November 6 closed the career of one of the best-known medical men in the West Country. Aged 74, he had been in charge of the department of pathology at the South Devon and East Cornwall Hospital, Plymouth, for 30 years until his retirement in 1952.

Eric Wordley was born in London in 1887. From Oldenham School he went on to Cambridge, where he had a much-valued year studying biochemistry under Sir Frederick Gowland Hopkins. He qualified from St. Thomas's Hospital in 1912 and graduated M.B., B.Ch. in the following year. After holding several resident appointments at St. Thomas's, including that of resident anaesthetist, he left the hospital to serve with distinction in the R.A.M.C. throughout the first world war, and was awarded the Military Cross. He then returned to St. Thomas's first as medical registrar and then as assistant bacteriologist under the late Professor Dudgeon, with whom he wrote a number of papers. He took the M.R.C.P. in 1918, proceeded M.D. in 1923, and was elected F.R.C.P. in 1936.

Dr. Wordley moved to Plymouth in 1922, where he established a rapidly expanding pathological department in the South Devon and East Cornwall Hospital. Beside his laboratory work he was in great demand at the bedside because of his shrewd judgment and wide knowledge. At the Annual Meeting of the B.M.A. in Plymouth in 1938 he was a vice-president of the Section of Pathology, Bacteriology, and Immunology. He published many papers on a variety of subjects. In his later years it was no uncommon experience to see a young man, airing his knowledge of the recent literature, being handed a paper written by Wordley on the same subject many years before.

The volume of pathological work increased nearly a hundredfold during Wordley's time in Plymouth, but without any increase in the size of the laboratory and with very little extra equipment. Much of the work had to be ruthlessly pruned to the bare essentials, and few people realized how much the brusqueness of his refusals was the measure of Wordley's distaste for having to cut down the work. He poignantly regretted that the new laboratory, in the designing of which he played so large a part, was not completed before his retirement.

Only those who knew him best could fully appreciate Wordley's great charm. He read widely and could converse with authority on many subjects. His sense of humour, combined as it was with his clear integrity, made him a delightful companion, whether in his yacht, on the golf course, or at some social occasion. A visit to his home was always a pleasure. His technical staff were devoted to him, and there are few of those who worked with him who will not long remember his many unobtrusive personal kindnesses.

Dr. Wordley leaves a widow, a son, and two daughters. —M. R. T.

## GEORGE DEERY, M.B., B.Ch.

With the death on November 11 at Plymouth of Dr. George Deery, aged 75 years, the Association has lost yet another member who was well known throughout the South-west. His election to the Roll of Fellows of the B.M.A. in 1959 was a tribute to the value of his work for the medical profession.

George Deery was born on January 18, 1886, the son of Mr. Andrew Deery, who was prominent in the public life of County Tyrone. He studied medicine at the Queen's Colleges of Galway and Belfast, graduating M.B., B.Ch. from the Royal University of Ireland in 1908. He went to Plymouth in 1912 and was engaged in a busy general practice, for many years single-handed, until his retirement in 1940. In addition to this he devoted much time to local medical affairs, serving for many years on the old panel and insurance committees and taking an active part in the work of the B.M.A. He was chairman of the Plymouth Division from 1931 to 1933 and honorary secretary from 1942 to 1960. In recognition of these and other services he was elected a Fellow of the Association in 1959. He had also held the office of president of the Plymouth Medical Society. Up to the time of his death he still continued to take an interest in medical affairs, serving as treasurer of the local medical committee.

In the first world war Dr. Deery saw service with the R.A.M.C. in the Middle East. During and after the second world war he continued to do valuable work even after his retirement from active practice, holding the post of honorary secretary to the local medical war committee and serving as chairman of the local recruiting board and later of the National Service boards. After the coming into operation of the National Health Service in 1948 he was chairman of the local medical committee for 10 years.

Outside his professional work Dr. Deery was an active member of the Presbyterian Church, which he served as a Presbytery Elder. His friendliness and sound advice on medical affairs will be long remembered by his colleagues. The death of his wife six years ago left him very lonely. The large gathering at his Memorial Service, including many general practitioners and representatives of all branches of medicine in the City of Plymouth as well as representatives of many other organizations, showed the respect in which he was held by the local community. To his two daughters we extend our sincere sympathy.—D. V. S.

## H. S. KANDER, F.R.C.S.

Mr. Herbert S. Kander, consultant surgeon in otolaryngology to the Coventry and Warwickshire Hospital and Gulson Hospital, died in Coventry on November 17 at the age of 50.

Herbert Sigmund Kander was born in Karlsruhe on February 27, 1911. With a strong medical family tradition, he studied medicine at the Universities of Vienna and Munich. Before graduation, however, he was forced to leave Nazi Germany, and came to England in 1933 at the age of 22. In spite of language difficulties his academic ability enabled him to matriculate, and he was accepted as a student at St. Mary's Hospital, where he qualified in 1937. After holding the post of house-surgeon at St. Mary's he at once began to interest himself in otolaryngology. During the next two years he held registrarships in the ear, nose, and throat departments of St. Mary's Hospital, Golden Square Hospital, and Queen Mary's Hospital in the East End, taking the F.R.C.S. in his stride in 1939.

The war years were spent in general practice in Stafford, where he maintained his interest in otolaryngology at the Staffordshire General Infirmary. In 1946 he was appointed consultant surgeon in otolaryngology to the Coventry and Warwickshire Hospital, and it quickly became clear that he was a man of outstanding ability. His surgical technique was scrupulously careful, and his results were first-class. His opinion was widely sought, and his kind and considerate manner endeared him to his colleagues and to his patients. He was especially interested in deafness, and his skill and organization of special clinics gave cause for much gratitude amongst the deaf in Coventry. Herbert Kander proved his fortitude in overcoming the difficulties of his interrupted medical studies, but it was the last ten years of his life which really showed up the sterling qualities of his character. Dogged by recurring ill-health and under constant threat of

a major hypertensive catastrophe, he never showed the slightest signs of bitterness. He continued to give the service so widely demanded of him: his charm, his sense of humour, and his lively enthusiasm were undaunted by "the slings and arrows of outrageous fortune." When, in the end, the inevitable happened, it came as a great shock to his colleagues and to his many friends and patients.

We shall all miss a gallant and lovable friend, and to his wife, who is also a doctor, daughter, and son (now a medical student at St. Mary's) we offer our sincere sympathy.—T. H. B.

### H. A. C. DAVIDSON, L.R.C.P.&S.Ed.

Dr. H. A. C. Davidson, who formerly practised in Couper Angus, Perthshire, died on October 15 in Dundee Royal Infirmary. He was 92 years of age.

Hugh Alexander Charles Davidson was born on May 11, 1869, at Buckies, Caithness, where his family had lived for many generations. Educated at George Watson's College and the University of Edinburgh, he qualified in 1893. For the next three years he was in practice in Halkirk, Caithness, and then moved to Couper Angus, where he remained until he returned again in retirement to his native county in 1939. His practice in Couper Angus was probably one of the largest country practices in Scotland, and for many years he managed it more or less single-handed, being well known for his courtesy, kindness, and sense of duty. He was fond of recalling the old days in Edinburgh when he was a medical student, and a few years ago he gave an entertaining address to a gathering of doctors in Perth reminiscing from the wide range of his experience as a country doctor. Fond of gardening, he was passionately attached to fishing, looking forward keenly to his annual holidays in Caithness or the Hebrides.

Dr. Davidson is survived by his wife, two sons, and two daughters, one of whom is a doctor. Two of his grandsons are also doctors, and a granddaughter is a medical student.

### P. R. RIGGALL, M.R.C.S., L.R.C.P.

Dr. P. R. Riggall, who practised in Grimsby for many years, died on October 31 at his home there after a long illness. He was in his 68th year.

Paul Rigauld Riggall was born on May 14, 1894, the son of the Rev. Marmaduke Riggall. Before qualifying from University College Hospital in 1916 he served in the Royal Navy during the first world war as a surgeon probationer and was torpedoed in the Mediterranean. After qualifying he became a captain in the R.A.M.C., serving in India. He held house appointments at University College Hospital and at the Northern Infirmary, Inverness, but thereafter his whole professional life was spent in general practice in Grimsby, where his integrity and intense devotion to his work will cause him to be greatly missed. From 1934–5 he was chairman of the Grimsby Division of the B.M.A. He was a member of a Lincolnshire Huguenot family, and leaves a widow and married daughter.

### J. R. SINTON, M.D., M.R.C.P.

The obituary of Dr. J. R. Sinton was published in the *Journal* of November 4 (p. 1227).

Mr. W. D. PARK writes: Rob Sinton was one of those rare people who despite his short life was an inspiration to all those who knew him. Good as he was as a physician, it is about him as a man I feel I must write. It was my privilege to be closely associated with him and his family and to see the remarkable fortitude and courage with which he bore long periods of ill-health and great suffering. I never heard him complain, but this was no passive acceptance of misfortune: it was a symbol of the depth of his complete faith and sincerity that made misfortune just another stepping-stone in his life's work. His was the spiritual strength of the true Christian, and his passing leaves us sadder but wiser and more humble men.

### R. A. BURNETT, M.B., Ch.B.

The obituary of Dr. R. A. Burnett was published in the *Journal* of November 4 (p. 1228).

E. V. G. writes: Having been a partner of Dr. Burnett I would like to record my personal regret at his death at the age of only 46. Born in Liverpool, he was the member of a Scottish family and was brought up in Perthshire, coming to Congleton in 1944, at first as an assistant and later as a partner in one of the largest practices in the district. He proved himself a very skilful practitioner, much devoted to his work, and very popular with his patients. He had great sympathy and human understanding and was an ideal partner in medical practice.

## Medico-Legal

### NEGLIGENT PSYCHIATRIC TREATMENT

[FROM OUR LEGAL CORRESPONDENT]

On November 22 the Court of Appeal dismissed the appeal of Dr. Theodor Alfons Werner, of Wimpole Street, against a judgment of Mr. Justice Barry awarding damages of £6,000 against Dr. Werner for negligence in psychiatric treatment given to his patient, Miss Alice Landau, of Talbot Road, Highgate (*The Times*, November 23). The facts of this case appeared in a report of the trial before Mr. Justice Barry (*Journal*, March 18).

Mr. Justice Barry found that Dr. Werner was guilty of negligence in introducing a social relationship into a course of treatment by "transference." Mr. Justice Barry had said that this was a tragic mistake, although probably done with the best will in the world: he absolved Dr. Werner from all Miss Landau's allegations of professional and sexual misconduct.

The Court of Appeal upheld Mr. Justice Barry's judgment that Miss Landau had established that Dr. Werner as a consultant physician was negligent in his treatment of her as his patient. Before her first course of treatment with Dr. Werner had ended Miss Landau had fallen in love with him. The most prudent thing for Dr. Werner to have done then would have been to refer Miss Landau back to her own doctor and to advise continuing the treatment with someone else. Instead Dr. Werner started a series of social contacts with his patient.

#### Definition of Negligence

It was the duty of a doctor to exercise ordinary skill and care according to the ordinary and reasonable standards of those who practised in the same field of medicine or surgery. The standard for the specialist was the standard of the specialists. A doctor was not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art. A doctor might be negligent if he tried a new technique but, as Mr. Justice Barry had said and as the Court of Appeal reiterated, he must justify it before the Court. If his novel or exceptional treatment failed disastrously he could not complain if it was held that he went beyond the bounds of due care and skill as recognized generally. Success was the best justification for unusual and unestablished treatment.

The medical evidence had condemned social contacts, and Dr. Werner had failed to convince Mr. Justice Barry that his departure from general practice was justified and was a reasonable departure in this young science.

Although there had been considerable argument whether Dr. Werner's treatment was the cause of a deterioration in Miss Landau's health, the Court of Appeal upheld the finding that on the probabilities the causation was established.

# Medical Notes in Parliament

## CURRENT LEGISLATION

[FROM OUR PARLIAMENTARY CORRESPONDENT]

### Health Visitors and Social Workers

The Health Visitors and Social Workers Training Bill had a poor reception when it appeared in the House of Commons for second reading on November 24. Its purpose is to establish training councils for each of these two branches of social welfare, which will set up national standards of training and approve courses for certificates. They will be linked by having the same chairman and some members serving on both councils. Apart from the Ministry of Health spokesmen, Lord BALNIEL (Hertford, Con.) was almost the only one who came to praise: he saw in this attempt to turn a haphazard occupation into a co-ordinated profession an important and significant reform. Mostly the Bill was criticized for the inadequacy of its financial backing, estimated to be about £25,000 for each council. Mr. KENNETH ROBINSON (St. Pancras North, Lab.), leading an opposition which found this grossly inadequate, on this occasion had a supporter in Dame IRENE WARD (Tynemouth, Con.), who condemned it as cheeseparing reliance on persons with a vocation. Mr. ENOCH POWELL regarded the Bill as a means to an end in the development of community services and rebutted any charge of niggardliness.

### Sexual Offences Bill Introduced

Two new Bills of potential interest to doctors have made their appearance in the back-bench M.P.s' ballot. These are a Bill to amend the law relating to homosexual offences, which is presented by Mr. L. ABSE (Pontypool, Lab.), with all-party backing; and a Bill to empower local authorities to provide meals and recreation for old people, presented by Mr. G. JOHNSON SMITH (Holborn and St. Pancras South, Con.), also with support in the other parties. Neither Bill won one of the coveted first places on the dates available for second reading, but both came out of the ballot early enough to become the second order of the day—the Sexual Offences Bill on March 9, and the other on December 8.

## FALL-OUT: PRESENT SITUATION

On November 23 simultaneous statements on fall-out were made in both Houses of Parliament. That in the Lords was by Lord HAILSHAM in his capacity as Lord President of the Council and Minister for Science; and that in the Commons was by Mr. DENZIL FREETH, Parliamentary Secretary for Science. Both statements concluded as follows:

*The Present Situation*

The Government is satisfied that no special measures are necessary to protect the health of any section of the population from the fall-out from nuclear weapons which have so far been exploded. Milk throughout the country is safe for children of all ages. The Government will, however, maintain in readiness its plans to give the public ample warning if danger threatens in the future and to provide safe milk for babies should the need ever arise.

## QUESTIONS IN THE COMMONS

### Clearing House for University Places

Mr. S. CHETWYND (Stockton-on-Tees, Lab.) suggested in a question to the Chancellor of the Exchequer on November 21 that he should consult the university authorities about establishing a central clearing house to facilitate a simpler and more orderly process for admissions of students to universities. Mr. SELWYN LLOYD pointed out that admission was a matter for the universities themselves, and they were already examining the possibilities of a clearing-house system. Mr. CHETWYND pressed the Chancellor, since he was responsible for finding most of the money for universities, to ask them to deal with this as a matter of urgency. Admissions were almost impossible this year and would be even worse in the future. Mr. LLOYD assured Mr. Chetwynd that what he had said—with which he agreed—would be noted.

Provisional figures collected at the beginning of the current session show, according to another reply by the CHANCELLOR, that there are 69,625 men and 23,192 women doing full-time courses in universities in England and Wales.

### "Strait Jackets" in Prisons

Mr. A. SKEFFINGTON (Hayes and Harlington, Lab.) asked the Home Secretary on November 23 to detail the general circumstances in which "strait jackets" were used in prisons, and whether appropriate treatment by tranquillizing drugs was used as an alternative. Mr. R. A. BUTLER stated that in accordance with Rule 49 of the Prison Rules, 1949, a loose canvas restraint jacket, of a pattern approved by the Secretary of State, in which the arms were held down the sides, might be used in prisons when it was necessary to restrain a prisoner suffering from mental disturbance to avoid his injuring himself or others, or damaging property, or creating a disturbance. It might only be used on medical grounds on the written order of the prison medical officer. If the jacket was kept on for a period of 24 hours (apart from short temporary releases) it must then be removed for at least one hour, and might not be re-applied without the authority in writing of a member of the visiting committee or board of visitors, or a commissioner or assistant commissioner. Standing orders enjoined that every effort must be made to avoid recourse to mechanical restraints, and full particulars of each occasion must be recorded and reported; these were summarized in the Commissioners' annual reports. Tranquillizing drugs might be used as an alternative in appropriate cases.

### Regional Services of Consultants

Mr. KENNETH ROBINSON asked the Minister of Health on November 22 to state the number of consultants, indicating whole-time and part-time separately, under contract to each regional hospital board on December 31, 1959, December 31, 1960, and at the most recent date for which figures were available. Mr. POWELL gave him the following figures for July 1, 1960. The next corresponding figures thereafter would be for September 30, 1961, which were not yet available.

| Regional Hospital Board | Whole-time Paid (Number) (*a*) | Part-time Paid (Number) (*b*) | Honorary (Number) (*c*) |
|---|---|---|---|
| Newcastle | 124 | 291 | 5 |
| Leeds | 83 | 257 | 1 |
| Sheffield | 118 | 304 | 12 |
| East Anglian | 68 | 132 | 2 |
| North-west Metropolitan | 173 | 568 | 32 |
| North-east " | 123 | 446 | 5 |
| South-east " | 132 | 478 | 12 |
| South-west " | 169 | 413 | 21 |
| Oxford | 57 | 167 | 4 |
| South Western | 79 | 286 | 8 |
| Welsh | 125 | 197 | 14 |
| Birmingham | 208 | 340 | 33 |
| Manchester | 93 | 379 | 11 |
| Liverpool | 68 | 248 | 25 |
| Wessex | 71 | 181 | 1 |

NOTES: (1) The figures exclude consultants holding locum appointments only. (2) Some consultants hold whole-time appointments shared between two or more regional hospital boards or between regional hospital boards and boards of governors of teaching hospitals: these consultants are included in column (*a*) under each of the regional hospital boards with which they are in contract.

### Inflammable Spectacle Frames

Mr. JAMES DANCE (Bromsgrove, Con.) asked the Home Secretary if he was aware that highly inflammable material was being used for spectacle frames, and if he would take action to prevent this, in the interests of safety. Mr. BUTLER stated in reply that cellulose nitrate was used in the

manufacture of some spectacle frames, but he was advised that for practical reasons it was not in all circumstances possible to use a non-inflammable substitute. Only one other case of spectacles catching fire besides that recently reported by Mr. Dance had come to notice since 1957.

### Hospital Medical Staffing Review

Mr. L. PAVITT (Willesden, West, Lab.) asked if the Minister of Health was able to give details of the machinery he was establishing to conduct the review of hospital medical staffing. Mr. POWELL said he could not yet add to the reply he gave on November 13. He would send Mr. Pavitt details as soon as they had been settled with the profession.

### Regional Appeals Committee

Mr. PAVITT asked what factors were taken into account by a regional appeals committee when deciding the grading of a post; and to what extent such a decision was made on the basis of duties to be performed, and on the ability of each incumbent to perform those duties, respectively. Mr. POWELL replied that grading was based on the duties actually performed, and was normally decided by reference to definitions laid down by the Whitley Councils. Ability was not an issue for the committee.

## Universities and Colleges

### UNIVERSITY OF ABERDEEN

Dr. R. E. Mackie has been appointed to a Lectureship in Mental Health.

### UNIVERSITY OF LEEDS

At a meeting of the University Court held on November 15, 1961, it was decided to confer a number of honorary degrees, including the honorary D.Sc. on Professor P. M. S. Blackett, F.R.S., professor of physics in the Imperial College of Science and Technology, London University, and dean of the Royal College of Science (Imperial College), and the same honorary degree on Professor Konrad Lorenz, M.D., Ph.D., vice-director of the Max Planck Institut für Verhaltensphysiologie, Seewiesen Post Starnberg, Germany. It is hoped that the degrees will be conferred at a Congregation to be held on May 23, 1962.

### UNIVERSITY OF BRISTOL

The following appointments are announced: Dr. D. R. Coles, part-time (formerly full-time) Lecturer in Medicine; Dr. B. L. Dowling, Dr. W. J. C. C. Rich, Dr. M. K. Tidman, and Dr. A. M. Wilson, Demonstrators in Anatomy; Dr. I. A. Hawkins, Assistant Medical Officer; Dr. D. B. Peacock, Lecturer (formerly Research Assistant) in Bacteriology.

Dr. D. Brynmor Thomas has resigned from the appointment of Demonstrator in Anatomy.

### ROYAL FACULTY OF PHYSICIANS AND SURGEONS

At the annual meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on November 6 the following office-bearers were elected: *President*, Dr. J. H. Wright; *Visitor*, Sir Charles Illingworth; *Honorary Secretary*, Dr. Gavin B. Shaw; *Honorary Treasurer*, Mr. R. B. Wright; *Honorary Librarian*, Dr. A. L. Goodall; *Representative on General Medical Council*, Professor D. F. Cappell.

### ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At a meeting of the general body of Fellows of the College held in Adelaide on October 11, 1961, the following were admitted to Fellowship of the College: *Under Article 44*, Dr. Ewan Murray-Will, of New South Wales, and Professor Rupert A. Willis, of Cornwall, England.

The following candidates, who were successful at an examination held in Australia, were admitted to Membership of the College on October 9, 1961: Kurt Aaron, J. H. Casey, and R. Gordon, of Queensland; R. B. Goldrick, R. W. Haber, L. B. Hardacre, C. I Johnston, P. H Miles, K. W. Perkins, and M. C. Rozenberg, of New South Wales; Helen Byrne, J. H. Coldbeck, B. S. Gilligan, F. W. Gurr, Priscilla Kincaid-Smith, A. Kucers, J. A. Mirams, and W. B Stephens, of Victoria; M. W. Begg, D. E. Dunn, M. W. Miller, and D. N. Phear, of South Australia; P. M. Connor and S. S. Gubbay, of Western Australia. *Under Article 37*, J. V. Hurley, of Victoria.

## Vital Statistics

### Radioactive Iodine in Milk

The average content of iodine-131 in milk from depots which are sampled daily (see *Journal*, November 25, p. 1445) fell from 117 $\mu\mu$c/litre in the week ended November 11 to 93 $\mu\mu$c/litre in the week ended November 18. According to a statement from the Agricultural Research Council (Press Notice of November 23) the extent to which iodine-131 is deposited may vary widely for several weeks after the detonation of nuclear weapons because of changing meteorological conditions. "However," the statement continues, "especially since cattle will derive less of their food from contaminated pastures as winter advances, there is now no likelihood that the bomb tests which have so far occurred will cause the levels of iodine-131 in milk produce in any part of the country to reach that which would make it unsafe even for very young children. Monitoring will continue so long as appreciable quantities of iodine-131 remain."

### Fatal Farm Accidents

During the first ten months of this year, 126 farmers, farm workers, and children lost their lives through accidents on farms. This is 17 more than the total for the whole of 1960. The deaths were caused in the following ways: tractors overturning, 42; run over by tractors or trailed equipment, 10; other accidents with tractors or associated equipment, 9; fall from loads, 6; other falls, including ladders, 3; electrocuted—contact with overhead cables, 2, with electric power equipment, 3; gunshot, 9; tetanus, 3; by animals—bulls, 4, other animals, 3; falling objects (bales, etc.), 9; other causes (drowned, poisoned, crushed by lorry, burned, Weil's disease from rats), 23. In making known these figures the Ministry of Agriculture, Fisheries, and Food points out that many of these deaths would not have occurred if good safety advice had been followed and needless risks not taken.

### Road Casualties in September

Of the 612 deaths in road accidents during September, 214 were pedestrians, 195 were drivers or passengers in cars or other vehicles, 158 were motor cyclists, scooter, or moped riders, and 45 were pedal cyclists. In addition, 7,731 people were seriously injured.

During the third quarter of 1961 the increase in the total number of road casualties compared with the corresponding period of last year was less than 1%: during the first quarter the increase was 5%.

### B.C.G. Vaccination

The Minister of Health has decided that after December 11, 1961, the only B.C.G. vaccine to be supplied by the Ministry will be freeze-dried vaccine. Local authorities have for the last few years had the choice of freeze-dried B.C.G. vaccine of U.K. manufacture or Danish liquid vaccine. Experience has shown that freeze-dried vaccine has considerable advantages so far as distribution and storage are concerned, and it is now used to a much greater extent than the liquid form—Ministry of Health Circular 30/61.

### Poliomyelitis in Hull

The total number of confirmed cases of poliomyelitis in the Hull outbreak amounted to 87 at the beginning of this week, no cases having then been confirmed for over a week. Arrangements have been made for Hull residents, under 40 years of age, who had their one dose of Type 2 oral vaccine during the "crash" immunization campaign in October and who have received no injection of Salk vaccine, to be offered immunization this week with trivalent oral vaccine. A second dose of trivalent vaccine will be offered in the middle of January, 1962.

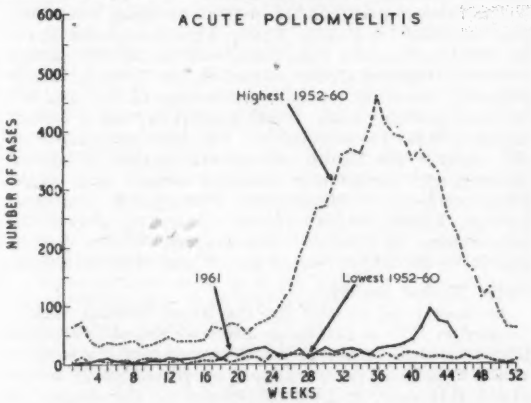
## Infectious Diseases

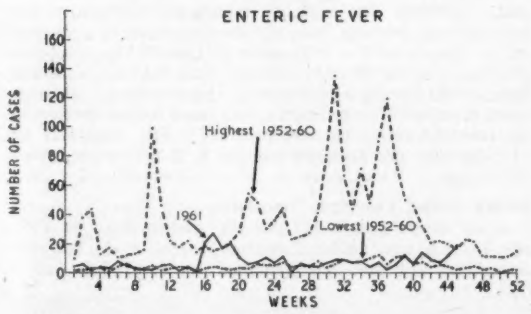
*Areas where the numbers of notifications were high in the latest two weeks for which figures are available.*

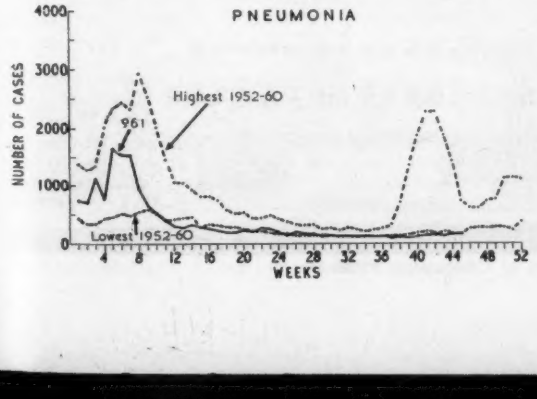
| | Week Ending Nov. 11 | Nov. 18 |
|---|---|---|
| **Typhoid Fever** | | |
| Lancashire ... ... ... .. | 1 | 7 |
| Salford C.B. ... ... ... ... | 0 | 6 |
| **Dysentery** | | |
| Essex ... ... ... ... ... | 6 | 29 |
| Leyton M.B. ... ... ... ... | 0 | 12 |
| Gloucestershire ... ... ... ... | 15 | 20 |
| Cirencester U.D. ... ... ... | 0 | 12 |
| Nottinghamshire ... ... ... ... | 3 | 21 |
| Worksop M.B. ... ... ... ... | 1 | 14 |
| Warwickshire ... ... ... ... | 25 | 39 |
| Coventry C.B. ... ... ... | 15 | 28 |
| Glasgow ... ... ... ... ... | 106 | 145 |

## Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.




# INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **November 11** (No. 45) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

* A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

| CASES | 1961 Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | 1960 Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
|---|---|---|---|---|---|---|---|---|---|---|
| Diphtheria .. | 2 | 0 | 2 | 0 | | 4 | 1 | 2 | 0 | |
| Dysentery .. | 338 | 25 | 215 | 15 | 8 | 443 | 40 | 164 | 5 | 6 |
| Encephalitis, acute | 3 | 0 | | 0 | | 3 | 0 | | 0 | |
| Enteric fever: | | | | | | | | | | |
| Typhoid .. | 7 | 6 | 0 | 0 | | 2 | 2 | 0 | 0 | |
| Paratyphoid .. | 12 | 0 | 0 | 0 | | 4 | 0 | 0 | 0 | |
| Food-poisoning .. | 116 | 13 | 7 | 9 | | 210 | 17 | 11 | 3 | |
| Infective enteritis or diarrhoea under 2 years .. .. | | | | 27 | 22 | | | | 10 | 40 |
| Measles* .. .. | 987 | 40 | 23 | 45 | 152 | 4,868 | 301 | 116 | 12 | 77 |
| Meningococcal infection .. .. | 14 | 1 | 7 | 0 | 1 | 27 | 5 | 5 | 0 | 2 |
| Ophthalmia neonatorum .. .. | 19 | 2 | 4 | 0 | | 17 | 2 | 3 | 0 | |
| Pneumonia† .. | 168 | 9 | 117 | 2 | 1 | 232 | 18 | 135 | 2 | 2 |
| Poliomyelitis, acute: | | | | | | | | | | |
| Paralytic .. | 28 | 3 | 0 | 0 | 2 | 8 | 0 | 0 | 0 | 2 |
| Non-paralytic .. | 17 | 1 | 0 | | | 0 | 0 | 1 | | |
| Puerperal fever§ .. | 146 | 29 | 24 | 0 | | 174 | 32 | 12 | 1 | |
| Scarlet fever .. | 374 | 38 | 73 | 10 | 13 | 435 | 23 | 67 | 33 | 16 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory .. | 332 | 53 | 52 | 17 | | 348 | 58 | 69 | 13 | |
| Non-respiratory | 51 | 7 | 15 | 4 | | 45 | 6 | 10 | 4 | |
| Whooping-cough | 194 | 21 | 29 | 4 | 9 | 835 | 69 | 83 | 2 | 45 |

| DEATHS | 1961 Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | 1960 Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
|---|---|---|---|---|---|---|---|---|---|---|
| Diphtheria .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dysentery .. | 0 | 0 | | 0 | | 2 | 0 | | 0 | |
| Encephalitis, acute | | 0 | | | 0 | | 0 | | | 0 |
| Enteric fever .. | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | |
| Infective enteritis or diarrhoea under 2 years .. .. | 7 | 0 | 0 | 0 | 3 | 10 | 1 | 0 | 1 | 1 |
| Influenza .. .. | 16 | 0 | 4 | 0 | 0 | 12 | 1 | 0 | 0 | 2 |
| Measles .. .. | | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Meningococcal infection .. .. | | 0 | 0 | | | | 0 | 0 | | |
| Pneumonia .. | 501 | 35 | 23 | 18 | 2 | 510 | 46 | 15 | 13 | 7 |
| Poliomyelitis, acute | 1 | 0 | | 0 | 0 | 1 | 0 | | 0 | 0 |
| Scarlet fever .. | | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory .. | 52 | 8 | 3 | 1 | 3 | 62 | 5 | 5 | 0 | 3 |
| Non-respiratory | | 0 | | 0 | 0 | | 0 | 1 | 0 | 0 |
| Whooping-cough | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Deaths 0–1 year .. | 326 | 41 | 28 | 10 | 21 | 331 | 37 | 37 | 18 | 5 |
| Deaths (excluding stillbirths) .. | 10,056 | 815 | 580 | 131 | 176 | 10,255 | 822 | 569 | 138 | 171 |
| **LIVE BIRTHS** .. | 14,273 | 1129 | 872 | 273 | 396 | 14,584 | 1294 | 961 | 288 | 330 |
| **STILLBIRTHS** .. | 300 | 27 | 20 | | | 270 | 20 | 20 | | |

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

# Medical News

**B.M.A.'s Hastings Lecture**

The B.M.A.'s Hastings Lecture, which furthers public education in health matters, is to be given in 1962 by Sir DAVID CAMPBELL, who has just retired as President of the General Medical Council. His speech is expected to concern some aspect of medical ethics and their bearing on the public. A departure from precedent is that the lecture will be given as part of the programme of the B.M.A.'s Annual Meeting, to be held next year at Belfast.

**Sir Howard Florey, Hon.F.R.C.S.**

Sir HOWARD FLOREY, P.R.S., was admitted to Honorary Fellowship of the Royal College of Surgeons of England at the College's annual meeting in Sheffield on November 25.

**Dinner of Royal College of Surgeons at Sheffield**

Sheffield was the site of the third annual meeting of the Royal College of Surgeons of England to be held in the provinces. As a prelude to the business meeting the Annual Dinner was held in the Cutlers Hall. Professor DIGBY CHAMBERLAIN, the Senior Vice-President of the College, in proposing the toast of "The City and University of Sheffield" briefly traced the history of the College for those who were visitors. He was most grateful to the city and the university for their hospitality, and it pleased him as a Yorkshireman that a Yorkshire centre had been chosen by the College for this meeting. After Alderman A. W. STERLAND, Lord Mayor of Sheffield, and Dr. J. M. WHITTAKER, Vice-Chancellor of the University of Sheffield, had replied to the toast the Master Cutler, Mr. GARARD YOUNG, proposed the health of the College. He spoke of his pleasure in working with surgical colleagues in his appointment as Governor to the Royal Hospital and looked forward to the day when Sheffield would have finished the building of its new teaching hospital. In reply, Sir ARTHUR PORRITT, P.R.C.S., emphasized the importance of the College as a stimulus in improving surgical standards throughout the country: equally the value of its research was now beyond dispute. Finally he expressed the thanks of the College to Mr. KENNEDY CASSELS for his many years of invaluable service as Secretary to the College.

**Nuffield Institute of Comparative Medicine**

It is hoped that work on the first stage of the Nuffield Institute of Comparative Medicine will start in June next year. (See *Journal*, May 14, 1960, p. 1492.) The new building will adjoin the offices of the Zoological Society, on the Outer Circle of Regent's Park, and will provide a new meeting-room for the Society on the ground floor as well as housing the Institute's main laboratories and other accommodation at upper levels. The building will lie immediately over the tunnel which links the main and middle gardens of the Zoo. (Architects: Llewelyn Davis and Weeks and John Musgrove.) The Institute's programme will include: support for the Cardiovascular Studies Group's research on arterial diseases in wild and domestic species and on the blood, in health and disease, of as many species as possible; the establishment of a Comparative Cardiovascular Registry and reference service, with facilities for contact through W.H.O. with overseas workers, and with the Cardiovascular Registry at the Walter Reed Institute, Washington; and the seeking of financial support.

**Bureau of Hygiene and Tropical Diseases**

Dr. CHARLES WILCOCKS has retired from the directorship of the Bureau of Hygiene and Tropical Diseases. He joined the Bureau as assistant director in 1938 and became director in 1942. His successor is Dr. H. J. O'D. BURKE-GAFFNEY, formerly assistant director (see *Journal*, September 2, p. 656). He is succeeded as assistant director by Dr. F. I. C. APTED, who served from 1941 to 1951 in the Colonial Medical Services in Sierra Leone and thereafter as Sleeping Sickness Specialist in Tanganyika. He was a member of the editorial panel of the *East African Medical Journal* from 1960.

**Central Middlesex Hospital**

A £10,000 Cardiothoracic Unit was opened at the Central Middlesex Hospital on November 24 by Sir HARRY JEPHCOTT, chairman of Glaxo Laboratories Ltd. The unit, which comprises a biochemical and physiological laboratory, clinical and radiology rooms, library, and offices, has been built through the generosity of local firms and friends of the hospital. Dr. HORACE JOULES and Dr. K. P. BALL will be in clinical charge. Research will be conducted on coronary diseases (with Professor J. N. MORRIS), bronchitis (with Dr. C. H. WOOD), and respiratory failure (with Dr. E. J. MORAN CAMPBELL).

**Medical Research Council of Ireland**

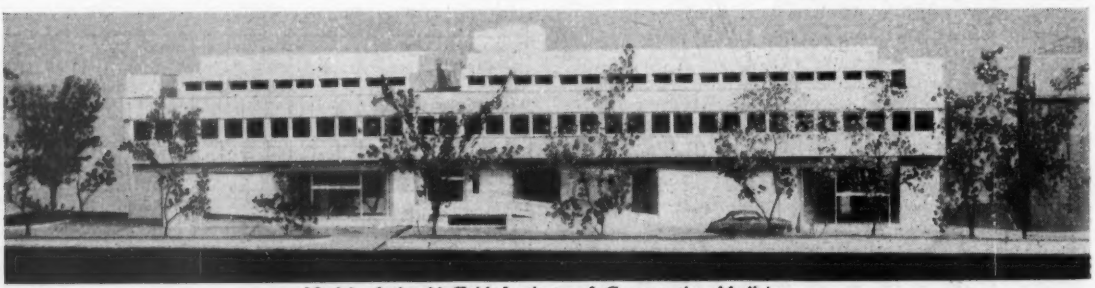
The Council spent £52,717 in 1960, of which administration accounted for £3,430. Research grants (with the figures for 1959 in brackets) were distributed as follows: general research, £18,618 (£13,104); chemotherapy research, £20,541 (£22,687); research on cell metabolism, £5,685 (£4,520); perinatal mortality study, £4,443 (£5,951); a total of £49,287 against £46,262 the year before. The increased grant from the Minister for Health was devoted mainly to clinical research, and substantially increased support went to the Departments of Medicine and Therapeutics, University College, Dublin, at St. Vincent's Hospital, and to the Departments of Medicine and Surgery, Trinity College, Dublin, at the Royal City of Dublin and Meath Hospitals.

**Royal Medical Society**

An appeal for support for the Royal Medical Society, founded in 1737 in Edinburgh and described as "the oldest medical student society in the Commonwealth," was made at the Presidents' Annual Dinner on November 23 by the Guest of Honour, Sir DERRICK DUNLOP. "The society," he said, "is rather like a proud, intelligent, very active, and beautiful old Duchess, who is, however, much impoverished and in consequence a trifle down at heel." The immediate problem is money for the upkeep of the fabric, furnishings, library, and heating of the society's present home. An even more serious future problem is the need to find money for an enforced move to new premises. The appeal is for £50,000, and the Society's address is 7 Melbourne Place, Edinburgh.

**British United Provident Association**

In its annual report for the year ending June 30, 1961, the B.U.P.A. announces substantial progress in the last year. Subscription income has increased by more than half a



Model of the Nuffield Institute of Comparative Medicine.

million pounds from £3,504,000 to £4,027,000. Nearly 85% (£3,397,000) of this last sum was paid out in claims—an increase of £280,000. Reserves have increased by nearly £300,000 to over £1,200,000 and the market value of investments by nearly £800,000 to £4,360,236. Membership has increased by 42,085 to 404,784, and it is estimated that, with dependants, B.U.P.A. is shielding more than 900,000 individuals.

**New Private Nursing Home for Birmingham**

A 48-bed nursing home for private patients is being planned for Edgbaston in Birmingham by the Nuffield Nursing Homes Trust, a charity associated with the British United Provident Association. An appeal has been launched with a target of £300,000, and the Trust has agreed to match pound for pound to a limit of £100,000 the total reached by local donations; £60,000 has already been raised. Inquiries about the appeal may be addressed to Mr. J. J. GRACIE, LL.D., c/o Room 8, P.O. Box 360, Edgbaston, Birmingham 15.

**The College of General Practitioners**

A large number of distinguished guests were entertained by the College of General Practitioners at its annual dinner on November 24. The Minister of Health, Mr. ENOCH POWELL, M.P., proposing the health of the College, said that the 10-to-15-years plan for the hospital service also included general practice. The future of the latter was bound up with the former. He hoped that in his training the general practitioner would have a longer association with the hospital service—an association which should continue throughout the whole of the G.P.'s life. The College of General Practitioners had been a great force in preventing the decay of general practice. In a witty and charming response, the President of the College, Dr. G. F. ABERCROMBIE, discovered that "Minister cuts acacia" was the anagram of the College's motto—cum scientia caritas. The specialists in medicine, surgery, and obstetrics provided the "scientia" and the general practitioner the "caritas." Lord COHEN, who replied for the guests, observed that medical science had become an advanced technology. But he was pleased to find that the opium and gentian represented in the College's new arms were still available in prescribable form. Dr. H. GUY DAIN also spoke.

**Jerusalem Medical School**

The Friends of the Hebrew University of Jerusalem held a dinner on November 23 in support of the medical school in Jerusalem. Lord NATHAN was in the chair. Dr. K. J. MANN, Director-General of the Hadassah Medical Organization in Israel, made an eloquent plea for funds: "We are part of a people where quality is emphasized." This was in reply to a toast by Dr. CHARLES HILL, M.P., who, describing a recent visit to Israel, said that Hadassah was one of the latest and most magnificently staffed hospitals he had seen. Lord COHEN urged support for the medical school in Jerusalem: "The economic stability of Israel," he said, "depends on the health of its citizens."

**Wingfield Music Club**

The Wingfield Music Club of Great Britain and Northern Ireland, details of whose next concert are given in this week's Coming Events column, was founded eight years ago by Mr. H. LYON with the aim of helping physically handicapped children to overcome their disabilities by mastering a musical instrument. Even severely spastic children have learned to play the violin or piano, those with an arm amputation the violin or 'cello, and asthmatic children wind instruments demanding breath control. Dr. HELEN WATSON, a general practitioner in Walthamstow, and Dr. IAN FLETCHER (Roehampton) are among the vice-presidents of the club. Doctors who would like to have more details of the scheme or those who wish to donate instruments should write first to the General Secretary, Mr. A. HUGGETT, 50 Belle Vue Road, Walthamstow, London E.17. (LARkswood 7076.) A recent grant from the Carnegie Trust enables some help with fares to be given to club members who do not live in London.

**Housing for the Disabled**

▶ Ideas for improving house planning for the disabled were demonstrated at the Building Exhibition held at Olympia at the end of last month. Particular attention was paid to avoiding changes of level, and to the planning of kitchens and bathrooms. A conference, "Architectural Design for the Disabled," was organized in conjunction with the demonstration by the National Fund for Research into Poliomyelitis and Other Crippling Diseases.

▶ The National Fund in association with the Royal Institute of British Architects has founded a research fellowship for studying the design of equipment, fittings, and buildings for the disabled. It is hoped that this will enable the R.I.B.A. Technical Information Service to publish a handbook for architects giving authoritative guidance on designing for the disabled.

**National Spastics Society**

The National Spastics Society will offer a reduced rate to members of the B.M.A. when it raises the general subscriptions to its publications next year. The special rates will be £1 a year for the *Cerebral Palsy Bulletin*, and £2 for *Little Club Clinics in Developmental Medicine*, instead of £3 and £4. The Society is publishing a third edition of its catalogue of *Films on Child Neurology and Cerebral Palsy* as a free supplement to the December issue of the *Cerebral Palsy Bulletin*. The catalogue includes articles on how to organize a film show and how to import and export scientific films. Non-subscribers may buy the catalogue (price 5s., or $1) from the Society, 12 Park Crescent, London W.1, or from the Executive Editor, 29 Hadlow Road, Tonbridge, Kent.

**Review of Medical Staffing of Scottish Hospitals**

The committee set up to review the medical staffing structure in Scottish hospitals is as follows: *Chairman:* Dr. J. H. WRIGHT, P.R.F.P.S.G.; *members:* Dr. F. D. BEDDARD, Dr. J. BRUCE DEWAR, Professor D. M. DOUGLAS, Mr. J. B. HUME, Dr. A. K. M. MACRAE; *Secretary:* Mr. R. R. W. Stewart (Glasgow Royal Infirmary Board of Management).

**Association of Clinical Biochemists**

The following officers have been elected for 1961–2: *president,* Dr. A. L. LATNER; *chairman,* Mr. H. VARLEY; *honorary treasurer,* Dr. R. GADDIE; *honorary secretary,* Dr. J. H. WILKINSON, Westminster Medical School, Horseferry Road, London S.W.1.

**World Federation of Neurosurgical Societies**

Professor EDUARD BUSCH (Copenhagen) has been elected President and Dr. A. EARL WALKER (Baltimore) Secretary of the Federation, and Mr. D. W. C. NORTHFIELD (London) Secretary for the Third International Congress of Neurological Surgery which is to be held in Copenhagen in 1965.

**Whittington Hospital Research Prizes**

Prizes of £25 have been awarded to Dr. JOYCE BURKE for a paper on "Pyelonephritis in Infancy and Childhood" and to Dr. N. J. GROSS for one on "Splinter Haemorrhages." Dr. JUNE ARNOLD's paper on "The Geriatric Service and the Community" and Dr. G. J. HEAP's on "Wound Infection after Appendicectomy" were highly commended.

**Change of Address**

The Medical Sickness Annuity and Life Assurance Society, Limited, and its subsidiaries, the Permanent Sickness Society Insurance Company and Medical Sickness Finance Corporation, have moved to 7–10 Chandos Street, Cavendish Square, London W.1 (Tel.: MUSeum 1686).

**"Family Doctor"**

The December issue of *Family Doctor* is now available, price 1s. 6d. It contains articles on widows and orphans, by Dr. FELIX BROWN; on the common cold, by Dr. M. L. BYNOE; on women over 40, by Dr. M. P. HUPPERT; and on the Munchausen syndrome, by Dr. F. R. C. CASSON.

## COMING EVENTS

**Osler Club.**—Joint meeting with Francis Bacon Society, December 6, 8 p.m., Gray's Inn. Speakers: Commander MARTIN PARES, R.N., Sir GEOFFREY KEYNES, Mr. A. DICKSON WRIGHT.

**Christian Medical Fellowship.**—Mr. S. G. BROWNE, "Medical Research—a Challenge to Christian Doctors," December 6, 6.30 p.m. See advertisement p. 61.

**Wingfield Music Club of Great Britain and Northern Ireland.**—Orchestral concert, December 10, 3 p.m., Lloyd Park Pavilion, Lloyd Park, Forest Road, Walthamstow, London E.17. All welcome. No tickets, collection taken.

**B.M.A. (Glasgow and West of Scotland Branch) Glasgow Division.**—Four live closed-circuit colour-television demonstrations, December 12, 13, 14, relayed from Southern General Hospital to Berkeley Hall, St. Andrew's Halls. Subjects: "Clinical Psychiatry," "Strokes," "Dermatology," "Chest Diseases." Admission by ticket only from Honorary Secretary, Glasgow Division, 9 Lynedoch Crescent, Glasgow C.3.

**Royal Society of Medicine.**—Children's holiday lectures, daily (2.30 p.m.) January 1–5. Details from Assistant Secretary, R.S.M., 1 Wimpole Street, London W.1.

**Chest and Heart Association.**—Conference, "Stroke Rehabilitation," January 11, 2–4.30 p.m., Royal Faculty of Physicians and Surgeons, 212 St. Vincent Street, Glasgow. Details from C.H.A., Scottish Branch, 65 Castle Street, Edinburgh 2.

**Health and Tuberculosis Conference.**—Sponsored by Chest and Heart Association with co-operation of Federal Government of Nigeria, March 26–31, 1962, University College, Ibadan, Nigeria. Charter plane leaves London on March 24, 1962. Details from Conference Secretary, C.H.A., Tavistock House North, Tavistock Square, London W.C.1.

## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

### Monday, December 4

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. H. E. Huxley: Mechanism of Muscular Contraction.

SOCIETY FOR MEDICAL AND DENTAL HYPNOSIS.—At Royal Society of Medicine, 8 p.m., Dr. Desmond F. O'Neill: Hypnosis in Stress Disorders.

### Tuesday, December 5

BIRMINGHAM AND MIDLAND MEDICAL ART SOCIETY.—At Birmingham Medical Institute, 8.30 p.m., Mr. John Woodward: Looking at Pictures.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. B. T. Donovan, Ph.D.: Timing of Puberty.

LONDON UNIVERSITY UNION SOCIALIST SOCIETY MEDICAL GROUP.—7 p.m., Four-Party Forum on the Welfare State. Speakers, Mr. Timothy Joyce (Liberal), Dr. J. D. Mabon (Labour), Mr. A. Tiley (Conservative), and Dr. Michael Kapoport (Communist).

MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Clinical Sciences Building, York Place, 4.30 for 5 p.m., Professor L. N. Pyrah: Some Aspects of Renal Calculi.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—8.30 p.m., FitzPatrick Lecture by Dr. K. D. Keele: Evolution of Clinical Methods in Medicine—(3) Impact of Science on Clinical Methods.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Mr. Denis Davey: Prediabetes and Pregnancy.

UNIVERSITY COLLEGE LONDON.—At Anatomy Theatre, Gower Street, W.C., 1.15 p.m., lunch-hour lecture by Dr. H. Kalmus: Biological Time-keeping.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. I. R. McCaul: Surgery of Parkinsonism.

### Wednesday, December 6

BIRMINGHAM MEDICAL INSTITUTE: MIDLAND MEDICAL SOCIETY SECTION.—At Selly Oak Hospital, 8.30 p.m., clinical meeting.

●CHRISTIAN MEDICAL FELLOWSHIP.—At 26 Portland Place, London W., 6.30 p.m., Mr. S. G. Browne: Medical Research—A Challenge to Christian Doctors.

INSTITUTE OF BIOLOGY.—At Lecture Theatre, British Museum (Natural History), Cromwell Road, London S.W., 5.15 p.m., Darwin Lecture in Human Biology by Dr. J. M. Tanner: Human Growth in its Comparative and Evolutionary Aspects.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. K. V. Sanderson: Histology—Cellular Naevi and Melanomas.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. M. Paneth: Prognosis of Mitral Stenosis.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Surgery of Calculi.

LONDON AMATEUR BOXING ASSOCIATION.—At British Railways Film Unit, Savile Row, W., 8 p.m. meeting of Medical Advisory Panel. Talk by Mr. W. E. Tucker: "Athletic Injuries," with film sequences.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University Medical School, 4 for 4.30 p.m., Dr. G. Komrower: Management of Congenital Adrenal Hyperplasia.

MIDLAND MEDICAL SOCIETY.—At Selly Oak Hospital, Birmingham, 8.30 p.m., clinical meeting.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—7.30 p.m., Mr. M. P. Earles, B.Pharm., M.Sc., F.P.S.: Early Scientific Studies of Drugs and Poisons.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. K. Fotherby: Use of Steroid Hormone Investigations in the Diagnosis of Disease (II).

QUAKER MEDICAL SOCIETY.—At Small Meeting House, Friends House, Euston Road, London N.W., 8 p.m., Lister Lecture by Sir Russell Brain, Bt.: Medicine in the New Renaissance.

RADCLIFFE INFIRMARY OXFORD.—At Maternity Lecture Theatre, 5 p.m., The Medical Consilium will commemorate the Bicentenary of the publication of J. B. Morgagni's "De Sedibus Morborum," 1761-1961.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. S. A. Heald: Public Relations and Food Hygiene.

### Thursday, December 7

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. F. Kingsley Sanders, D.Phil.: Infective Nucleic Acids and Virus Synthesis.

HONYMAN GILLESPIE LECTURES.—At Anatomy Theatre, University New Buildings, Teviot Place, 5 p.m., Dr. John Richmond: Observations on Haemolytic Disease.

LEWISHAM GENERAL HOSPITAL.—5.45 p.m., Dr. C. A. Holman: Haemolytic Disease of the Newborn.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., joint meeting with Liverpool Psychiatric Club. Symposium: Alcoholism. Speakers, Dr. J. S. Madden, Dr. W. H. R. Cook, and Dr. W. L. Selkirk.

MEDICAL ASSOCIATION FOR THE PREVENTION OF WAR.—At Friends' House, Euston Road, London N.W., 6.30 p.m., Mr. Henry Usborne: A Federation of Nations.

NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, Oxford, 8.30 p.m., Mr. Dillwyn Evans: The Relapsed Club Foot.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—8.30 p.m., FitzPatrick Lecture by Dr. K. D. Keele: Evolution of Clinical Methods in Medicine—(4) Vision in Clinical Medicine.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor J. B. M Roberts: Spina Bifida and the Urinary Tract.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5.15 p.m., Sir Paul Mallinson: postgraduate demonstration in psychiatry.

### Friday, December 8

CLINICAL SOCIETY OF BATH.—At Teaching Department, Royal United Hospital, 8 for 8.30 p.m., Sir W. Russell Brain: Cervical Spondylosis.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. D. Barlow: clinical demonstration.

KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.

PLYMOUTH MEDICAL SOCIETY.—At North Friary House, 8.30 p.m., Professor C. D. Calnan: New Forms of Contact Dermatitis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Mr. Walpole Lewin: Recent Advances in the Treatment of Head Injuries. (2) 4 p.m., Professor C. H. Stuart-Harris: Respiratory Vascular Disorders.

### Saturday, December 9

●CAMBRIDGE UNIVERSITY POSTGRADUATE MEDICAL SCHOOL.—At Addenbrooke's Hospital, Cambridge, symposium on Pain. *Morning session*, 10.30 a.m., Dr. G. S. Brindley: Neurophysiology of Pain; 11.45 a.m., Professor F. H. Shaw (Melbourne): (*a*) Response of Animals to Drugs in the Normal and Anaesthetized States; (*b*) Management of Cancer Pain with Opiates and Tetrahydroaminacrine. *Afternoon session*, 2.30 p.m., Professor T. C. Gray: Analgesic Supplementation of General Anaesthesia; 3.30 p.m., Dr. H. R. Youngman: Phenol Nerve Block in the Treatment of Intractable Pain.

SHEFFIELD REGIONAL PSYCHIATRIC ASSOCIATION.—At Whiteley Wood Clinic, Sheffield, 11 a.m., Professor Desmond Curran: Defence of Amnesia in the Criminal Court.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Bernstein.**—On November 4, 1961, to Julia M. (formerly Levi) Bernstein, M.B., B.S., D.P.H., and Ronald Bernstein, of 65 Highgate West Hill, London N., a brother for Mark Jonathan—John Daniel.

### DEATHS

**Apthorp.**—On November 19, 1961, Hugh Llewellyn Apthorp, M.D.

**Atlee.**—On November 11, 1961, Charles Nelson Atlee, M.D., D.P.H., D.P.M., of Finchley, London N.

**Buckley.**—On November 10, 1961, at Cheltenham, William Buckley, M.R.C.S., L.R.C.P.

**Clements.**—On November 19, 1961, at the White House, Molescroft, Beverly, E. Yorks, Ernest Clements, M.B., Ch.B., aged 83.

**Deery.**—On November 11, 1961, George Deery, M.B., B.Ch., of 7 Hartley Park Gardens, Plymouth, aged 75.

**Griffith.**—On October 29, 1961, Adrian Nicholas Griffith, M.B., B.Ch., F.R.C.S., aged 33.

**Hishon.**—On November 2, 1961, at Bournemouth, Denis Joseph Hishon, M.B., Ch.B.

**Homan.**—On October 28, 1961, Thomas Delapere Homan, M.D., late of Mallow and Blarney, Co. Cork.

**Lewis-Badgett.**—On November 9, 1961, at his home, Manor Lodge, Egerton Street, Mossley, near Manchester, David Philip Lewis-Badgett, L.R.C.P.&S.

**Macdonald.**—On October 29, 1961, at his home, 22 New Street, Stornoway, Isle of Lewis, Donald Macdonald, M.B., Ch.B.

**McNickle.**—On November 12, 1961, Lawrence Cradock McNickle, M.D., of Public Hospital, New Zealand.

**Pringle.**—On November 6, 1961, at his home, 16 Charles Cope Road, Orton, Longueville, Peterborough, George Loraine Kerr Pringle, *M.C.*, M.D., aged 92.

**Vinter.**—On November 9, 1961, at Walton-on-Thames, Surrey, Sydney Garratt Vinter, M.R.C.S., L.R.C.P., D.P.H., aged 97.

**Welton-Hogg.**—On November 11, 1961, in Wellington, New Zealand, Robert Welton-Hogg, M.B., B.S.

**Wordley.**—On November 6, 1961, at Windrush, St. Mawes, Cornwall, Eric Wordley, *M.C.*, M.D., F.R.C.P., aged 74.

# Any Questions?

*We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.*

### Hypoplasia of Corpus Cavernosum

**Q.**—*I have a patient who states that since childhood his penis has deviated to the left. The left corpus cavernosum throughout its length is only half, or less, the diameter of the right corpus. I presume the condition is due to a congenital hypoplasia of the left corpus. Is there any operative treatment which would remedy this defect, since he naturally complains of great difficulty at sexual intercourse?*

**A.**—The fact that the penis has deviated to the left since childhood would indicate that this is due to a congenital failure of development of one corpus cavernosum. However, it would be important to determine by careful clinical examination whether in fact the deviation was not due to a thrombosis in the opposite corpus cavernosum giving an impression that the normal side was much smaller. If, as seems most likely, this is a problem of congenital failure of development nothing can now be done for the primary defect. However, it might well be possible to correct the chordee on erection by suitable plastic surgery, and it would be advisable to obtain a plastic surgeon's opinion.

### Ionization in Rheumatoid Arthritis

**Q.**—*Is ionization of value in treating an inflammatory flare-up in one knee of an elderly patient with rheumatoid arthritis?*

**A.**—Ionization is of no value in treating an inflammatory flare-up of rheumatoid arthritis. It is of only very doubtful value in the treatment of chronic joint disease.

### Tetanus Immunization

**Q.**—*We live in an area where tetanus is prevalent, and we are attempting to give everyone complete immunization. So far we have given two doses with an interval of six weeks between them followed by a booster dose in about three years. Is it essential that three injections should be given in the initial immunizing programme?*

**A.**—The correct course for primary immunization against tetanus consists of three injections of tetanus toxoid with intervals of 6–12 weeks between the first and second doses and 6–12 months between the second and third doses. Reinforcing doses (say, two or three) at five-yearly intervals are recommended to maintain the immunity resulting from the primary course. The schedule suggested in the question is unsatisfactory: there should be three injections in the primary course, and the third must be given between 6 and 12 months after the second. Although some latitude is possible with intervals between doses, there are certain limits which immunologists have found by experiment and experience to be necessary.

### Intercourse After Prostatectomy

**Q.**—*For how long after prostatectomy for benign hypertrophy of the gland is sexual intercourse inadvisable? Do the ejaculatory ducts reconstruct themselves and reopen into the urethra? Is hydrocele more likely to develop after prostatectomy?*

**A.**—The length of abstinence from intercourse would depend entirely on inclination. If the vasa had not been tied spermatozoa will still appear in the prostatic urethra during orgasm, but owing to the absence of an internal sphincter ejaculation tends to occur back into the bladder rather than forward through the tonic external sphincter. It should be remembered that even if the vasa are tied spermatozoa may appear in the ejaculate or the urine for a considerable while after the operation.

There would appear to be no relationship between development of a hydrocele and the operation of prostatectomy.

### Reaction to Pyrvinium

**Q.**—*A boy was given pyrvinium in a single dose for the treatment of enterobiasis. The following day he developed a red, oedematous, vesicular condition affecting the right periorbital tissues resembling strongly the fixed drug eruption one may see after sensitivity to phenolphthalein. Associated with the rash was pyrexia and rigors. The condition subsided slowly on prednisolone and antibiotics. Has pyrvinium been known to produce a fixed drug eruption before?*

**A.**—Pyrvinium either as the chloride or the embonate has been shown to be as effective in the treatment of threadworms as the more commonly used piperazine.[1] In the usual therapeutic dose no serious toxic effects have been reported. Nausea and vomiting occur in a few cases, and the drug gives both the stools and the vomitus a red colour. In laboratory studies in animals bone marrow depression has been reported in one species, and it is therefore recommended that the drug should not be given for more than a few days and that it should be used cautiously in patients with any hepatic or renal disease. So far as I am aware a reaction of the type described has not been reported previously, but it is of some interest that a similar type of reaction has been described in a case where piperazine was given for the treatment of threadworms.[2] In this case the reaction also occurred on the second day, but the patient had been given a previous course of piperazine three months before and thus was presumably sensitized. It would therefore be of interest to know whether in the present case there had been any previous administration of pyrvinium.

REFERENCES

1 Bumbalo, T. S., Plummer, L. J., and Warner, J. R., *Amer. J. trop. Med.*, 1958, 7, 212.
2 Hill, B. H. R., *N.Z. med. J.*, 1957, 56, 572.

### Allergy to Pertussis Vaccine

**Q.**—*At the age of 4½ months my youngest child received his first diphtheria–tetanus–pertussis vaccine. Two hours later he became cyanosed, unconscious, and showed signs of peripheral circulatory failure. He recovered slowly, becoming conscious within an hour and being apparently normal 24 hours after inoculation. What risk would be attached to further immunization procedures at his present age of 20 months?*

**A.**—This severe reaction was probably due to the pertussis vaccine component. Although this information is not given, the child may have a personal (or family) allergic history and therefore would not be a suitable subject for pertussis vaccine. Although often a child who has reacted to a first dose does not react to the second or third dose of triple antigen it is reasonable to suggest that at the age of 20 months, in view of the severe reaction to the first dose, he need not be subjected to the risk of a reaction to the second dose of triple antigen. At his age he has passed the period when whooping-cough is most serious and sometimes fatal, and if he were to catch whooping-cough it would most probably be a mild or moderate attack. A wiser procedure would be to commence anew a primary course of immunization against diphtheria and tetanus. First, however, because of his age, it would be advisable to do smallpox vaccination followed at least three weeks later by polio vaccination—two doses of inactivated (Salk-type) vaccine four to six weeks apart. A month later, all being well, diphtheria and tetanus vaccine (DT/Vac) could be given—two doses four

to six weeks apart; a third dose would be necessary later, preferably about school-entry (4 to 5 years). If oral polio vaccine becomes available DT/Vac could be given at the same time as oral polio vaccine—thus shortening the immunization schedule.

### Face Masks

**Q.**—*Do masks prevent the spread of infection from the nose and mouth, particularly when the wearer has a cold? If so, what is the most efficient and practical type to use?*

**A.**—Masks can greatly reduce the dissemination of particles of secretion by coughing, sneezing, or talking. If a simple gauze mask is used filtration is inadequate unless it consists of many layers. A better type consists of only two layers of gauze with a layer of impermeable material between them, which can be either a plastic film or simply paper. Such a mask deflects the stream of air but traps a high proportion of the fluid particles in it. Successful use demands frequent renewal. In particular, a mask used during ward work should not be displaced and replaced by the wearer, since it then becomes a means of transferring possibly infected secretion to the hands.

### Female Haemophilics

**Q.**—*Can a sex-linked recessive condition—for example, classical haemophilia (haemophilia A)—occur in a female if a carrier woman marries an affected man? Textbooks repeatedly state that the condition occurs only in males.*

**A.**—Haemophilia can occur in girls who are homozygous for the gene for haemophilia as a result of the marriage of a carrier (heterozygous) woman with an affected (hemizygous) man. The first case in this country appears to have been described by Treves, in 1886,[1] in a girl aged 6 whose haemophilic father had married his mother's sister's daughter. Later investigation of this Essex family has shown that the bleeding diathesis in it was classical haemophilia.[2] More recent examples have been described by Merskey[3] and Israëls.[4] This is not, however, the only mechanism by which a girl may have classical haemophilia. In some families heterozygous females may show a haemorrhagic tendency and A.H.G. deficiency,[5 6] while other individuals who, though phenotypically female, have the genotype XO or XY[7] could manifest haemophilia if their X chromosome bore the gene concerned; and some affected girls apparently homozygous for the gene concerned,[8] though born to heterozygous mothers married to a normal father, must be assumed to have derived both their X chromosomes from their mother's mutant-bearing X chromosome.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### Genetic Damage from Radiotherapy

**Q.**—*A young married woman of 24 has an osteoclastoma of the left ilium. It is too large to remove, and she is having a course of radiotherapy. In view of the situation and the possibility of scatter affecting the left ovary and causing genetic damage she has been advised not to have any children for five years. How grave is this danger, and can we be certain that after five years, subject, of course, to no recurrence of the tumour, this danger will no longer remain?*

**A.**—In a woman aged 24 all the germ cells in the ovary will be at the oocyte stage. On exposure of the ovary to *x*-ray therapy the probability of induction of genetic change will be approximately the same for each cell. From this angle, therefore, there is no point in the advice given to delay having children. The radiation dose to double the natural mutation rate may be around 50 r.

The advice given would have been more appropriate for a man, when continuous production of mature germ cells (spermatozoa) occurs in adult life from gonial cells. Delay of a month or so would allow discharge of irradiated sperm in which the frequency of chromosomal damage would, on present evidence, be much higher than in new crops of spermatozoa derived from irradiated spermatogonia.

## NOTES AND COMMENTS

**Prophylactics for the Maldives.**—Dr. T. R. F. RAW (Horley, Surrey) writes: Under "Any Questions?" (October 28, p. 1163) a question is asked: "What is Maldive fever?" I am sure this is mite typhus fever. I was an R.A.M.C. physician to a small Indian general hospital during 1943–4 stationed on the island of Gan, one of the Maldive islands. This was when the jungle on Gan was being cleared to form an air-strip, and I believe it is now a permanent R.A.F. base. In the course of six months I had over 200 cases of mite typhus fever with a mortality of six per cent. The soldiers of the island garrison were employed clearing the jungle for the airstrip and were bitten by the mites attached to the leaves of the trees. There was a large rat colony, which was, of course, the reservoir of the infection. All cases gave a strong positive agglutination response to *Proteus* OXK and negative to OX19 and OX2. Apart from this disease the islands were very healthy. I never saw a case of endogenous malaria, but beware of falling coconuts during high winds and sea snakes on the coral reefs. The climate is perfect—about 85° F. (29° C.) all the year round. I wonder if typhus still occurs on Gan now.

Professor W. E. KERSHAW (School of Tropical Medicine, University of Liverpool) writes: I write in connexion with the question on prophylactics for the Maldives: "What is Maldive fever, and is there any drug which prevents it?" Maldive fever is the local name for scrub-typhus, for which chloramphenicol is both curative and suppressive. When I was in the southernmost atoll during the war there was no difficulty in distinguishing scrub-typhus from dengue, though scrub-typhus had been erroneously identified as dengue in another archipelago in the Indian Ocean. Malaria and scrub-typhus were then the most common fevers; any others were mere curiosities.

OUR EXPERT replies: Dr. Raw's and Professor Kershaw's notes are of very great interest and value, and I have no doubt that what they saw on Gan in 1943–4 was mite-born typhus. Dr. Raw's note emphasizes the point made in the reply to this question to the effect that a number of entities are referred to by local designations, and the final point in this question of whether typhus is still present in Gan underlies the way in which non-permanent endemicity and epidemicity may give rise to designations which outlive the persistence of the disease in that area. Clearly wherever possible such terms should no longer be used but should be replaced by scientific terminology.


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